

# ANNALS OF SURGERY

VOL. 110

OCTOBER, 1939

No. 4



## TRANSACTIONS OF THE AMERICAN SURGICAL ASSOCIATION

MEETING HELD IN HOT SPRINGS, VA.

MAY 11, 12, 13, 1939

### ADDRESS OF THE PRESIDENT

#### THE DEVELOPMENT OF NATIONAL SURGICAL SOCIETIES WITH THE ADVENT OF MODERN SURGERY\*

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MEMBERS of the American Surgical Association and Guests: In opening the Scientific Session of this annual meeting I must first express my great appreciation of the honor of being chosen to serve as your presiding officer. During my 22 years of membership in this Association, I have attended all of the meetings except those of 1918 and 1926, at which times I was in Europe. The experiences which I have had during these years in listening to the presentations, in occasional appearances on the programs and in participating in the general fellowship of the Association are among the most treasured of my professional career.

For a topic of discussion I have chosen the development of national surgical societies with the advent of modern surgery. It is hoped that in addition to the general interest which other societies may have for us, their procedures may be found helpful in outlining the course of our own Association.

There was little need for special surgical societies of national scope until the advent of antisepsis since the advances in surgery up to that time were relatively slow and its practice was extensively concentrated in the large cities which were adequately served by local societies. Then, as progress almost overnight became exceedingly rapid, the demand arose for organizations to meet the needs of the profession of entire nations or of groups of

\* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

nations with a common language. First came the establishment of general surgical societies, to which this discussion will be limited, and then followed the societies of the surgical specialties as those fields were developed.

The oldest existing national surgical organizations are the Royal College of Surgeons of Scotland founded in 1505 and the Royal College of Surgeons of England founded in 1800. But they differ from surgical organizations which have followed outside the British Commonwealth in that their primary function has been to serve as examining and certifying boards. They have never conducted annual surgical congresses for the discussion of scientific topics, their educational activities being confined almost entirely to lecture-ships. In consequence, the Surgical Section of the British Medical Association, established in 1867, became the important British forum for the discussion of modern advances in Surgery. It remains an active organization with an annual attendance ranging up to 400 members. A special surgical society, The Association of Surgeons of Great Britain and Ireland, was founded as late as 1920, chiefly by the initiative of Lord Moynihan. Its membership is limited to 250 surgeons, 200 of whom are active members and 50 associate members. They meet annually for three days the first week in May in one of the university cities, every third meeting being in London. Forenoons are devoted to papers and afternoons to operations and clinical demonstrations. Its membership is drawn largely from the surgeons of the teaching hospitals and there is little discrimination between general surgeons and surgical specialists.

The first modern society for the surgeons of a nation, or better stated, for the surgeons of any nationality using a common language, was the German Society for Surgery, established in 1872. Prior to that time the meeting place of German surgeons had been in the surgical section of the Society of German Natural Philosophers and Physicians. It was eventually recognized as being inadequate for the needs of the growing specialty and at the annual meeting in 1871, Gustav Simon took the initiative for the organization of a separate society. Consequently, on the invitation of Simon, Langenbeck and Volckmann, a meeting was called for the following April and the German Society for Surgery was formed. It has always met annually in Berlin for three and one-half days during the week following Easter. There are four forenoon, one evening and three afternoon sessions and the annual dinner.

The policy adopted for membership was very inclusive. It was to be unlimited in number; anyone specializing in surgery, using the German language and recommended by two members of the society, was eligible for election subject to approval of the Executive Committee. In consequence the membership grew rapidly from 81 for the first meeting to 651 in 1896, to 2,236 in 1914, and to 2,599 in 1933. After that it had declined to 2,264 in 1937, when the last statistics were published.

In contrast to this inclusive policy for membership, an exclusive policy for administration and program was adopted and has been continued. Langenbeck, the then recognized leader of German surgery, served as president



for the first 15 years, since which time the office has usually been occupied by one who has served for one year only. During the 68 years of its existence, only three men have served as secretary, to which office has been entrusted great responsibility in the selection of the programs. Gurlt occupied the position for 28 years, Körte for 31 years, and Borchard has now served for nine years.

An endeavor is made to obtain for the program each year the most important advances in the entire field of surgery, which are presented to the society meeting as one body. There are usually 75 to 85 speakers. The presentations average ten minutes in length with the exception of certain special dissertations, which are longer. Discussions are numerous and criticisms free. The transactions were issued as separate publications, for the first 50 years, but have since appeared annually in one volume of the *Archiv für klinische Chirurgie*.

The influence of the German Society for Surgery on surgical progress has been enormous. In the first place, it has reached a great many persons. Because of its inclusive policy, its membership and the attendance at the congresses have been large, including many surgeons from states adjacent to Germany. Because of its lengthy programs and of the preference given to original work, irrespective of whether accomplished by one of the younger or older members, a remarkably high percentage of the advances which the German speaking peoples have made in surgery have first been presented at these annual congresses. This fact is obvious to anyone who examines the Transactions, which have been widely read, or who reads Friedrich Trendelenburg's "The First Twenty-Five Years of the German Society for Surgery." At the same time, the scholarship of the presentations has been of an order that had served well to popularize the recent advances made elsewhere. It is safe to say that by pursuing the path advocated at the beginning, its large membership and extensive programs of high quality have led to much greater accomplishments on the part of its members and to much greater influence on German and world surgery than would have resulted from pursuing the path then advocated by Billroth, who preferred a small, intimate body which would issue no publications.

Surgery in France long centered to an unusual degree in Paris. The Royal Academy of Surgery, of glorious memory, existed from 1731 to 1793, when it, along with the other academies, was overthrown by the revolutionists with the famous explanation that "France no longer had need for men of learning." There was no further organization until 1843, when the Society of Surgery of Paris was formed. Its success from the first was great, but with the advent of the new era it is commendable that its own members took the initiative in the establishment of the French Surgical Association in 1884. The stated aims of the Association were "to advance the science of surgery and to establish scientific bonds between the savants and the practitioners of surgery." Membership was to be inclusive, and was made open to all French speaking surgeons regardless of nationality. It provided for a congress lasting six days which has been held annually in Paris

during the first half of October. Two hundred fifteen members were elected at the first congress and the number increased rapidly so that for several years the membership has been in the vicinity of 1,200.

The sessions are held during the afternoons, the forenoons being principally devoted to attendance at clinics. At each of three sessions, the discussions are limited to two topics, usually related. An essayist is chosen for each topic one year in advance and his presentation is usually lengthy and scholarly. Then follow numerous short, prepared discussions, sometimes totaling 20 in number. At the other three sessions, miscellaneous papers are presented from the general field of surgery and its specialties. The congress has been an important implement for dissemination of surgical knowledge especially in France and the other Latin countries. A volume of transactions is published annually.

The Italian Surgical Society was formed in 1882, along lines somewhat similar to those of the German and French societies. Its annual meetings are held in Rome during the month of October. In 1937, its membership had grown to 721.

Surgical societies similar to those of Germany, France and Italy have been established in most of the other states of Europe and in South America and Japan. Since large inclusive medical societies like the American, Canadian and British Medical Associations, with their sections on surgery, do not exist in other countries, their large surgical congresses are of great national import for progress in surgery.

In the United States and Canada, a mixed course has been pursued as compared with Great Britain and continental Europe. A Section on Surgery of the American Medical Association has existed since 1860, and the attendance at the sessions in recent years has averaged more than 1,000 members. A surgical section has existed in the Canadian Medical Association since 1869, and recent attendances have reached as high as 300 members, when the meetings have been held in the large eastern cities. These sections have played an important part in the dissemination of knowledge to the general body of surgeons of the two countries.

Contrary to the situation in other parts of the world, two societies, the American Surgical Association and the American College of Surgeons, have come into existence to meet the special surgical needs of the United States and Canada. This resulted principally from the course that has been pursued by the American Surgical Association since soon after its establishment. The original plan, as reviewed so dramatically two years ago in the "dialogue" between President Evarts A. Graham and Founder Samuel D. Gross, appears to have been for a large society somewhat similar to those which have developed in Europe. Its membership was limited to 100 at the time of formation in 1880, and there were 91 fellows at the time of the first scientific meeting in 1882. But, the advisability of making it easy to enlarge the membership was immediately realized, as Doctor Gross stated in his opening presidential address, in 1883, that the Council was recommending an increase from 100 to 150 fellows to be voted at that meet-

ing. The measure was apparently adopted but after the retirement of Doctor Gross the policy of expansion into a large society as surgery grew was not pursued and the limit for active membership remained as low as 150 until 1934 when, as a result of repeated appeals for enlargement, provision was made to increase it gradually over a period of five years to the present number of 175.

As a result of this extremely conservative, almost inflexible, policy with reference to membership during a 51-year period of unprecedented growth in population, in surgery and in number of surgeons, the Association gradually became more and more exclusive. This left an ever increasing demand for a surgical organization to meet the needs of the large number of surgeons who were not being adequately cared for by the surgical sections of the American and Canadian Medical Associations.

Franklin H. Martin, seeing this golden opportunity, started the Clinical Congress of Surgeons in 1910, and, in 1913, organized out of it the American College of Surgeons. It was started with 1,064 fellows and the number was rapidly increased until at the present time it amounts to 11,639, representing all fields of surgery, gynecology and obstetrics. In proportion to the number of physicians in the two countries, the membership from the United States is about twice as numerous as that from Canada. It serves both as a certifying body, by the granting of fellowships, and as an educational body through its annual five-day Clinical Congress, its sectional meetings and its publications. Both functions are definite drawing cards for membership and there is an average attendance at the annual Clinical Congress of about 3,000 fellows.

Since the American College of Surgeons and the American Surgical Association are now both well established societies, they should be continued, each to serve the purposes for which it is best adapted. The American College of Surgeons, in addition to other functions, should aim at imparting knowledge through its congresses to a large body of the surgical profession, correcting its tendency to be too inclusive, so that it will not foster the performance of surgery by some who are inadequately qualified. On the other hand, the American Surgical Association, which is now destined to remain a relatively small organization, should only admit to fellowship those who are engaged more specifically in the advancement of the science and the art of surgery. Most men of this class are connected with medical schools, but all should be included who demonstrate their ability to make significant contributions to surgery whether by clinical or laboratory investigation, and whether they are connected with teaching or nonteaching institutions. With such a representation, it would be possible, at the annual meetings, to present the great majority of the advances made in surgery in the two countries to a group who, in turn, would make the greatest use of the information gained in practice, teaching and research. In other words, the Association should operate as a forum which fosters surgical education and research throughout the United States and Canada.

It might be said that this has been the end for which the Association

has always striven. The Constitution states: "The object of this Association shall be the cultivation and improvement of the science and art of surgery, the elevation of the medical profession and such other matters as may come legitimately within its sphere." But the Association does not function in these respects to the extent that it should in view of the significant name that it bears. The main reason for this is that the limited membership excludes too many of the ever increasing number of surgeons who are qualified to take part in the programs and who should profit by its proceedings. To repeat what has often been pointed out, the competition is so stiff that men are usually not elected to fellowship until they are mature surgeons unless they have accomplished outstanding investigations. The age limit is 30 years, but at present the youngest fellow is 38 years old and the average age of the active fellows is 53.9 years. That means that most of the presentations are of a sound and reliable nature, emanating from men of seasoned judgment and accomplished surgical technic. This type of work should always comprise a large part of the program. But most contributions that are notable for their fundamental originality, whether in the field of clinical or laboratory investigation, come from the younger surgeons, the majority of whom are now automatically excluded from fellowship. The present arrangement, whereby some of them appear on the program by invitation either as co-author or alone is helpful but is no real solution of the problem.

Also, the influence of the Association on the medical schools is not as widespread as it should be. There are 66 medical schools in the United States classified as acceptable by the American Medical Association, and nine medical schools in Canada. Of these, 27 in the United States and seven in Canada have no faculty member who is an active fellow of the Association. No plea is made for a wholesale admission of the teachers of these medical schools or of those schools which already have representation. However, a survey would undoubtedly disclose many suitable candidates in both groups.

The matter of sectionalism calls for discussion in this connection. The older, more prosperous and more densely populated sections are, in general, the seats of the better supported and more fully developed institutions, whose staffs have the greatest representation in this Association. But the newer and less densely populated districts must maintain institutions to serve their own needs and this they usually do as efficiently as their means permit. If the influence of the Association is to be disseminated as widely throughout the two countries as should be the case, somewhat greater allowance should be made for handicaps of these sections than is now made, and fellowship should be extended to more members of the staffs of their institutions than would be granted to those of similar accomplishments in more advantageous communities. The Association would then assist, more than at present, in elevating their standards. It is noteworthy that every medical school of any important European country has faculty representation in its national surgical association and that eligibility usually extends to those of the lower ranks.

Since the main purpose of the Association is the advancement of surgery, it should not shut itself off too much from the rest of the surgical world. If the advancement of the fellows themselves should ever become too prominent an aim, it might be accused, as was the Royal Society of Physicians and Chirurgeons of London just before its demise in 1905, of existing more for the exclusion than for the election of members.

Obviously, if more men are to be admitted from the ranks of the educators and investigators in surgery, the limit on membership in the Association will have to be appropriately increased and kept readily flexible. With the expressed goal of the Association kept firmly in mind, it would then be possible in the course of a few years to bring up the membership to a point of maximum efficiency. In order to adjust for the increased number of suitable papers that would be offered, a considerable proportion of them might be limited to ten minutes, as is the case with many special societies. In many cases all that is essentially new about presentations may be given before an audience of specialists in the field in ten minutes. With such an arrangement, even with the present freedom of discussion, it would be possible to present at least 45 papers during three full days instead of 32 as at the present meeting.

It is worth while for us to glance at what is being done correspondingly by our colleagues in the field of internal medicine. The youthful American Society for Clinical Investigation with 200 members, and the Association of American Physicians with 225 members, meet annually the first week in May at Atlantic City, the former for one day and the latter for the two following days. There is an extensive overlap in membership and in attendance of the two coordinated societies. Also, the meetings are open and in a large hall so that a great many nonmembers, mostly young and attached to departments of internal medicine, are welcome and privileged to be present. There are presented 25 to 30 ten-minute papers, principally of experimental work, by the Society for Clinical Investigation, and 45 to 50 fifteen-minute papers principally of clinical work by the Association of American Physicians. By this arrangement about twice as many papers are presented in the three days before three or four times as many persons as in the meetings of our Association.

The American Surgical Association has maintained a standard of integrity for membership which is one of its finest traditions. It is well expressed by the motto selected by Malgaigne for the Society of Surgery of Paris: "Truth in the science, morality in the art," and it should be safeguarded in any policy of future expansion. I want to conclude with my conviction that: If provision were made for proper gradual enlargement of the membership, to comply with the available talent, the Association would enter a period of growth in which it would maintain its tradition for excellence of performance, stimulate more fellows to increased productivity, and steadily widen its much needed influence in the entire world of surgery.



## REPAIR OF CRANIAL DEFECTS BY CRANIOPLASTY \*

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THE EARLIEST INSTANCE of cranioplasty in man to which reference can be found is a case reported by J. van Meekren, in 1670, in which a bone from a dog was used to successfully repair a cranial defect in a man. The graft was successful, but was removed because of the opposition of the Church to the use of an animal's bone in "marring God's image." This case was reported by Grekov, in 1901, and is quoted here from Pankratiev<sup>90</sup> (1933), the original literature not being available.

Over 200 years passed before any other reports of plastic operations performed upon the skull were published. During this interval much work on bone grafting in general had appeared. With the work of Ollier,<sup>98</sup> in 1859, in grafting bones from one animal into another, all the information necessary for the satisfactory repair of cranial defects was available. Several decades passed before it was used. Macewen<sup>79</sup> reported the reimplantation of antiseptic bone fragments into the cranial defects from which they were removed after the defect had been cleaned up and the fragments treated with bichloride of mercury. He had used this procedure since 1873 with fair success. The same year Burrel<sup>20</sup> and Guerix<sup>49</sup> reported the implantation of bone buttons following trephining, Guerix on animals and Burrel on a human. The next year, Gerstein<sup>44</sup> used Macewen's method successfully in one case and Ballou<sup>5</sup> described the satisfactory outcome of a case in which he reimplanted the trephine button. Senn,<sup>114</sup> reporting on the use of antiseptic, decalcified bone to repair defects, made the statement that this method was excellent for the repair of cranial defects but gave no cases. The cases that he described all followed osteomyelitis elsewhere in the body.

Seydel,<sup>115</sup> in 1889, reported a case of depressed fracture of the left parietal area in which, after the fragment had been removed, the defect was repaired by a graft several millimeters thick chiseled from the tibia with the periosteum intact. This graft was placed in saline, divided into pieces, and placed on the dura in a mosaic with the periosteum downward. The area was covered with a dry iodoform and bichloride dressing and then with silk. On the fifth day, the graft seemed healthy and closely adherent to the dura, the whole surface being pink. At this time the skin was closed. The patient made an uneventful recovery. With the report of this case the present day technics of plastic closure of the skull started. Von Jacksch<sup>61</sup> felt that the drawback to Seydel's method was the necessity of two operations upon the same patient. He re-

\* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

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ported a case in which a goose skull treated with ether and bichloride of mercury was used to fill in a cranial defect. The result was a solid, but slightly depressed, area.

W. Müller,<sup>94</sup> in 1890, outlined a case in which he repaired a skull defect by taking a flap of skin, pericranium and outer table and swinging it into the defect in a manner similar to the old method for the reconstruction of the nose that had been known and used in India for centuries. König,<sup>68</sup> a little later in the same year, advocated the use of twin flaps. One flap contained the skin and what was left of the pericranium from the site of the defect and the other the skin, pericranium and outer table taken from an adjacent area in such a way that the bases of the flaps were opposite to each other and they might be transposed. The flap with the outer table then covered the defect and the skin flap filled in the area from which the outer table had been removed. The small openings left by the transposition of the flaps were closed by Tiersch grafts. This seemed to be a very adequate procedure for the repair of small defects but was not sufficiently elastic to be applicable to large ones. It is interesting to note that in this same paper he suggested that when trephining is necessary, a flap of skin, periosteum and outer table be formed. The trephine opening is made in the inner table and later covered with the outer table and skin as the flap is sewn back into place. This was probably suggested by the work of Wagner<sup>134</sup> (1889) on osteoplastic craniotomy.

In 1891, von Hinterstoisser<sup>58</sup> reported a case of traumatic epilepsy with a cranial defect that he repaired with celluloid. Von Frey,<sup>42</sup> in 1894, reported a case successfully closed with a celluloid plate and finally, in 1895, Fraenkel<sup>39 40</sup> reported his work on closing cranial defects with celluloid plates and cited three cases, one with a follow-up of three-quarters of a year; another died following the implantation of a celluloid plate in a wound that was infected before operation and not entirely healed at the time of the operation.

Kümmell,<sup>70</sup> in 1891, made use of the method of Senn (1889), employing decalcified bone. He stated that he obtained good results but gives no statistics.

Schönborn,<sup>113</sup> in 1891, reported a case done by König's method in which he was able to fill in a defect that measured 14x3 cm. A year later, Tietze<sup>123</sup> (1892) described a case in which he repaired a defect by König's method but gives very little information.

In 1893, Booth and Curtis<sup>14</sup> reported the first attempt to fill a cranial defect by means of a metal plate. They used aluminum. The patient died ten days after operation.

Beck,<sup>7</sup> in 1894, outlined a case done by the König method and another done by a number of methods that all failed, although the patient finally had a spontaneous regeneration of bone. Czerny,<sup>27</sup> in 1895, reported that he had not had any success with celluloid plates, and that he had had trouble with one plastic of the König type because the patient had not had any diploe. One case done with a tibial graft was well after two years. One of the grafts introduced by the method of König had to be removed 18 months after operation

for another cause. It was found that the graft had formed a new inner surface. In the same year, von Eiselberg<sup>33</sup> reported eight cases, in five of which he used the Müller-König technic. All were in good condition two years later. Of three that were done with celluloid, two were in good condition one and three-quarters and four and one-half years later, while one still had a fistula at the end of four years. He discusses the indications for this operation in cases of posttraumatic epilepsy, stating that although he had had no complete cures, most of the patients were benefited, some greatly, and that he feels it to be indicated in cases of focal epilepsy as well as in cases where pain is a large factor. Nicoladoni,<sup>97</sup> in 1895, reported a single case done with the Müller-König technic, which he modified by sawing the graft off after he had chiseled a groove around the area that he wished to remove. He felt that this avoided the cracking of the graft that occurs when it is removed with a chisel and gave a solid graft that was preferable.

Gerster<sup>45</sup> (1895) repaired a defect of the skull with a thin gold plate. The case was followed for two and one-half years, at which time there was no demonstrable reaction to the metallic graft, and it was satisfactory in all ways.

Link<sup>77</sup> (1896) described three cases of celluloid cranioplasty, without adequate follow-up, and concluded that this method is advantageous for the closure of large cranial defects.

Berndt,<sup>9</sup> (1898) reporting several cases done by the Müller-König or tibial graft technic, had been able to follow one case of tibial graft that was in excellent condition after six years.

Grekoff<sup>47</sup> (1898) used a technic developed by Barth<sup>6</sup> (1896) in closing two defects with incinerated bone with apparent success, although the follow-up is not adequate.

Von Hacker,<sup>51</sup> in 1903, outlined a new method for the repair of defects. He cut around part of a pericranial flap, chiseled off the outer table under this flap, leaving it still attached to the flap, and then turned the flap over 180 degrees so that it came to lie over the defect with the bony side uppermost. He reported two cases done by this method and feels that it was applicable in many cases where the Müller-König method could not be used. In the same year, Bunge,<sup>19</sup> in Garre's Clinic, reported two cases that were repaired by periosteal osseous flaps that were so placed that they could be swung into the defect without turning them over, thus leaving the periosteal side outermost, and stitching it to the surrounding pericranium. These cases were followed for 10 and 14 months and were solid and smooth when last seen. He also detailed the case of a patient whose defect was repaired by a fresh osteo-periosteal graft from another patient. The graft was good three years later.

Keen,<sup>66</sup> in 1905, recommended the use of bone chips from the surrounding bone to fill in defects, and reported a case in which satisfactory repair was obtained in this way.

Stieda<sup>122</sup> (1905) described eight cases that were adequately followed. Two patients had two operations. Six Müller-König cranioplasties were all in good condition at the end of periods varying up to five years. One showed

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a small depression but it was solid. One case was cured of epilepsy. One repair, done by the von Hacker technic, was satisfactory for some time (?) following operation. One, done by the technic of Garre, was in good condition after four years. One case, repaired with a piece of boiled bone, developed a fistula after nine months and was reoperated. The defect was repaired by a tibial graft. Five years later this was solid, though the patient complained of occasional headaches.

Blecher<sup>10</sup> (1906) writing of celluloid cranioplasty, reported a case of his own and collected 11 from the literature, four of which had been unsuccessful. In the same year Borchard<sup>15</sup> reported three cases of cranioplasty: one with the pericranium alone was unsuccessful; one with von Hacker's method with the periosteum innermost was solid but some spurs had developed over the graft. Eight cases of osteoperiosteal flap, after Garre (Bunge), were all successful. Pringle<sup>107</sup> described six cases of celluloid cranioplasty, and found that they were unsatisfactory, one because of sepsis.

In 1907, Söhr,<sup>121</sup> from Garre's Clinic, reviewed their results to date and gives the work of Garre in more detail. He reports seven cases in which various kinds of osteoperiosteal grafts were used. In five, either one or two flaps from the outer table of the skull were moved into the defect. In one case, the graft was cut entirely free from the pericranium and stitched into the defect—this is the earliest record that we find of this type of operation that is now in common usage. One case was repaired by a separate osteoperiosteal graft of the outer table that was stitched into the defect with the bony side uppermost. He states that Lyssenkow developed the technic of turning the graft 180 degrees so that the bony side was outermost and that von Hacker did this later. He quotes work by Durante that we have been unable to find in the literature up until 1922, although referred to by other authors without adequate reference.

A case repaired with an aluminum plate was reported by Elsberg,<sup>34</sup> in 1908.

Leotta,<sup>74, 75</sup> in 1909, described a method that was adopted from Durante's technic of osteoplastic craniotomy. The whole thickness of the skin is taken, having attached to its under surface slivers of the outer table picked up by chiseling under the pericranium. The flap with these slivers attached is then freed at its base and displaced so that the portion containing the slivers of bone come to lie over the cranial defect. He states that one advantage of this technic is that it can be adapted to larger defects than the methods of von Hacker and Garre.

Righetti<sup>108, 109</sup> modified the methods of von Hacker and Durante by taking a periosteal flap with bone slivers attached and turning it 180 degrees to cover the defect. He reported five cases, using this method, that were in good condition from one month to six months after operation.

In 1916, Axhausen<sup>2</sup> returned to the osteoperiosteal graft from the tibia which he wedged into the defect with finger pressure. His conclusions from 27 cases were that this method was better in every way than the Müller-König.

Delageniere<sup>29</sup> perfected the technic of osteoperiosteal grafts from the tibia; he cut his grafts thin and put them over the defect, between bone and pericranium with the periosteum outermost. Occasionally he used a second layer placed in the defect with the periosteum toward the dura so that both sides of the repaired area were smooth. In a number of papers, from 1916 to 1935,<sup>30, 31</sup> he reported 104 cases with two failures, one of which was successfully reoperated.

In 1915, Morestin<sup>90, 91</sup> described the use of cartilage for the repair of cranial defects. He took his grafts from other patients for the most part, and reported no difficulty arising because of this. A year later, Gosset<sup>48</sup> detailed 32 cases done by this method, in which there were two deaths, both from bronchopneumonia. He placed the perichondral side innermost and held the graft in place by sutures. Other cases done with cartilage have been outlined by Auvray,<sup>1</sup> Leo,<sup>73</sup> Peraire,<sup>100</sup> Villandre,<sup>127, 128</sup> Laquiere,<sup>71</sup> Chutro,<sup>22, 23</sup> Leriche,<sup>76</sup> Boinet,<sup>12, 13</sup> Gilmore,<sup>46</sup> Beguoin,<sup>8</sup> Wilson,<sup>136</sup> Coughlin,<sup>26</sup> Hanson,<sup>53, 54, 55</sup> Munroe,<sup>95</sup> Julliard,<sup>63</sup> and Termier.<sup>124</sup>

Mayet,<sup>83, 84, 85, 86</sup> in 1916, again used a method of osteoperiosteal graft from the skull, a flap that was turned 180 degrees and stitched in place by wire or catgut. He felt that this method was much easier than any of the others, and reported 43 cases without adequate follow-up. Cazin,<sup>21</sup> the same year, operated upon 30 cases by a method in which he took a graft of skin, pericranium and outer table, or only pericranium and outer table, on a very long pedicle or with two pedicles and swung it into place with the bone side down. He states that the nourishment to this type of graft was adequate and probably better than that of the other methods.

Peraire<sup>101, 102, 103</sup> (1916, 1917, 1919) described 29 cases done with various methods, and got good results in all of them.

Estor<sup>36</sup> (1916, 1917) reported 100 cases of cranioplasty with gold plates. Two cases died of infection and two were infected and the plate had to be removed. In the septic cases, the plates were found to be in good position and firmly fixed. He found the patients liked the gold plates.

Villandre,<sup>127, 128, 129, 130, 131</sup> in a series of papers in 1916 and 1917, detailed 130 cases of cranioplasty done by different methods. He had his best results with osteoperiosteal grafts from the tibia. Less success followed in the cases that were repaired by placing calcium paste in the defect, hoping that the presence of the salts would act as a stimulant to new bone formation, as indeed was the case in half of the patients.

In reporting 10 cases of repair with osteoperiosteal flaps from the skull, Pflugrad<sup>104</sup> (1916) used the galea as part of the flap in four cases. The reason for this is not clear, unless it is that he used this method in larger flaps. One would think that the circulation of the skin would be badly interfered with, but his follow-up on these cases makes no note of this.

Westermann<sup>135</sup> (1916) recommended the use of the sternum as a graft for skull defects.

Babcock<sup>3</sup> (1917) used soup bone to repair defects. He was able to follow two cases for two years, at which time they were in good condition. This



method had been used before by Villandre and others. Villandre reported 23 cases with four failures; he used both human and animal bone.

In 1917, Brown<sup>17</sup> reported on the use of ribs in the repair of skull defects. He used only the outer half, leaving the inner half still in place. The notes on his cases are not adequate to judge his results, but here was a new method that gave promise of being very useful in the repair of large defects.

In 1917, A. Hofman<sup>59</sup> modified the technic of osteoperiosteal flap grafting by cutting an extra large piece of periosteum, part of which he folded around the bone from the outer table. Just what he hoped to gain by this is not quite clear. The viability of the bone might be improved in this way, but it would seem to be an efficient barrier to any fusion of the graft to the edge of the defect. He gave no follow-up on any of his cases.

Morison<sup>92</sup> (1917) reported 12 cases of tibia grafts in which the grafts were set into a slot cut in the edge of the cranial defect.

In a series of papers by Siccard, Dambrin and Roger,<sup>117, 118, 119</sup> from 1917 to 1919, and, later, Dambrin and Dambrin<sup>28</sup> (1936), the use of cadaver skull for cranioplasty was reported and 120 cases collected. The chief factors of importance were that they treated the bone with sodium carbonate and heat; then with xylol, then with alcohol and ether and finally sterilized it by heat. The bone was reduced in thickness until only the outer table remained and was then perforated freely. Their results were very satisfactory.

In 1920, Kreider<sup>60</sup> described an interesting method of cranioplasty that has a limited scope. At the time of injury, he takes the fragments of bone removed from the depressed fracture and tucks them under the skin of the abdomen. Then at a later date, when the scalp wound has healed and the bone proven to be free from infection, he transplants it back into the defect.

MacLennan<sup>80</sup> (1920) detailed the use of parts of the scapula, noting that, by taking a piece from the infraspinatus fossa the full thickness of the bone, a graft is obtained that has periosteum on both sides and is still fairly thin. Saito,<sup>112</sup> in 1925, reported two cases done in this way. In 1921, Pickerill<sup>105</sup> described a similar technic using part of the ilium.

Cornioly<sup>25</sup> (1929) outlined the use of a platinum plate that stayed in place for 14 months without any sign of reaction. Lluesma-Uranga<sup>78</sup> (1936) reported the use of silver wire woven into a meshwork to fill in defects.

Fagarasano,<sup>37</sup> in 1937, described the use of split ribs as grafts. He places them so that the normal curvature is inward regardless of which side the periosteum lays and places them in small slots in the bone, stitching them in place by using the pericranium.

Other authors who have used boiled or cadaver bone are: Boinet,<sup>11, 12, 13</sup> Pankratiev,<sup>99</sup> and Gurdjian.<sup>50</sup> Celluloid: Blecher,<sup>10</sup> Pringle,<sup>107</sup> and Erdheim.<sup>35</sup> Fresh bone from other patients: Rocher,<sup>110, 111</sup> Osteoperiosteal from the skull: Le Fur,<sup>72</sup> Frazier and Ingham,<sup>41</sup> Coleman,<sup>24</sup> Drevermann,<sup>32</sup> Sudhoff,<sup>123</sup> Bower,<sup>16</sup> Käfer,<sup>65</sup> Juvara,<sup>64</sup> Jones,<sup>62</sup> and Gurdjian.<sup>50</sup> Osteoperiosteal from the tibia: Nesselrode,<sup>96</sup> Gilmore,<sup>46</sup> Begouin,<sup>8</sup> Kerr,<sup>67</sup> Rocher,<sup>110</sup> Young,<sup>137</sup> Drevermann,<sup>32</sup> Brusken,<sup>18</sup> Termier,<sup>124</sup> Hadley,<sup>52</sup> and Fourmestraux.<sup>38</sup> From

ribs: Ballin,<sup>4</sup> Shuttleworth,<sup>116</sup> Brusken,<sup>18</sup> and Gurdjian.<sup>50</sup> Breast bone: Müller, P.<sup>93</sup> Ilium: Money.<sup>89</sup>

It is not possible to analyze the cases in the literature as thoroughly as one might wish, because of the lack of adequate follow-up, which we think should be at least nine months and, better, a year. On the other hand, it seems to be true that most of the failures occur early and the shorter period will catch the majority of them. The cases in the charts do not include all of those that we have collected. We have eliminated all reports of single cases after 1900 unless they are important. A number of reports of a few cases have been left out because of lack of enough information to make them useful.

In all, we have charted 1,385 cases, arranged according to the method used, in an attempt to ascertain which of the various methods is the best. The only figure from the entire group that is at all significant is the mortality rate, which is 0.73 per cent.

*Indications.*—There seems to be a happy accord among most of the authors as to the indications for cranioplasty and the only possible disagreement lies in the degree to which symptoms may be allowed to progress before operation is advisable. The indications are:

- (1) Severe headache and other symptoms of the syndrome of the trephined—dizziness, undue fatigability, vague discomfort at the site of the defect, a feeling of apprehension and insecurity, mental depression and intolerance to vibration.
- (2) Epilepsy, when the attacks originated from the injury that caused the defect.
- (3) Those cases in which there is danger of trauma at the site of the defect.
- (4) Cases that have an unsightly defect.
- (5) Defects that pulsate unduly or that are painful.

The contraindications are again pretty well agreed upon. They are:

- (1) The presence of any foreign body.
- (2) The presence of any possible infection in either brain or bone.
- (3) Increased cerebrospinal fluid pressure that is not easily reducible by lumbar puncture.
- (4) Pathologic changes in the cell count or chemistry of the fluid.

Cranioplasty should not be performed for some months after an injury unless the wound is undoubtedly clean. If there has been infection, it is not safe to attempt it in much less than one year's time. Some cases that have had osteomyelitis have given trouble several years after they were supposed to be free of infection. Delay allows the dura a chance to repair itself so that any infection at operation will remain extradural.

Among the authors who have written about the repair of cranial defects, Tuffier and Guillain<sup>126</sup> have had the opportunity of following the greatest number of cases. They conclude that the procedure is of little value except from

the cosmetic point of view. This opinion is at variance with that of the vast majority of writers.

*Technical Notes.*—There are several features apparent in reviewing the reported cases that are well accepted as important. The scar of the original injury should be in good condition. If it is not, there should be a preliminary operation to revise it and eliminate any danger of its breaking down from lack of an adequate blood supply or other cause. A very thin scar should be revised even if adequately nourished. When the defect is exposed, the dura should be well freed around the edge and any defects in it repaired by the use of fascial grafts. Following this the bone edge should be freshened by cutting it back until healthy oozing bone is reached. In cutting back the bone edge, the defect should be rounded as much as possible so that the graft will fit snugly. While freshening the bone, the pericranium should be carefully protected so that it will be intact and in good condition to use in holding the graft in position. The graft should be slightly larger than the trimmed defect to insure a snug fit. If this is not done, the pericranium will adhere to the dura and form a barrier to bone formation between the graft and the edge of the defect. If there has been any increase in intracranial pressure, great care must be taken to control it during the healing period, else it will lift the graft and prevent good bony union.

*Comparison of Methods.*—In general, it may be stated that the simplest methods are preferable and that methods entailing only one operative procedure are preferable to those necessitating two. These factors are not, however, the only ones that demand attention, as we must consider the results, insofar as that is possible, of the different methods. For example, it is well known, and admitted by all authors, that cranioplasties done with cartilage remain cartilaginous and the repaired area is never solid, but always has some "give." The fact that the cartilage is well tolerated (Beguoin,<sup>8</sup> Chutro,<sup>22</sup> and Morestin<sup>90</sup>), rarely absorbs (Chutro<sup>22</sup>); and that it forms a firm union with the surrounding bone (Mairano and Virano<sup>81</sup>) is, for the moment, of little importance. The important thing is that this method never brings about a firm, solid, bony closure, but tends to become more and more fibrocartilaginous as time goes on (Leriche<sup>76</sup>). If this fact is accepted, and cartilage is reserved for the closure of small defects where the importance of a rigid graft is not so great, it has a very definite place in the operative scheme. Its use for the closure of large defects is probably ill advised. Furthermore, in the case of cartilage, if there is not a piece available from another patient—and it appears that cartilage from other humans is perfectly tolerated (Morestin<sup>90</sup>)—we are faced with the necessity of a second operation to obtain the graft. But an osteoperiosteal graft from the external table of the skull, that may be either swung or thrown over into place, or taken separately and placed in the defect without connection with its original environment, will close it in a single operative session.

The various types of osteoperiosteal grafts from the outer table of the skull all have their application in the repair of different sizes of defects depending somewhat on the location of the defect and on the condition of the overlying

skin. It would seem to make little difference whether the bony or periosteal side of the graft is outermost, except that the bony side is more apt to be irregular. Whether the graft remains attached to the pericranium by a pedicle is of no importance. The possible blood supply from this source is poor at best, and we have had perfectly good results from grafts that were entirely separated from the pericranium.

The work of Gallie and Robertson<sup>43</sup> has impressed us with the importance of using bone that has as much cancellous tissue as possible in order that many viable osteoblasts are available. The diploic surface of the outer table of the skull seems to be a source for these, preferable perhaps to tibial grafts but probably not as good as rib grafts or grafts from the sternum. The use of split ribs, especially in the repair of defects that are too large for a graft from the skull, is a very sound method. The curvature of the pieces is just about right, and there are sufficient osteogenic cells present.

The use of celluloid, we think, is to be avoided. It is fairly well tolerated, but is objectionable on the following grounds: Unless a fairly thick piece is used, it is not rigid and fails in its purpose. Cases have been reported in which the graft has softened and become ineffective (Henschen<sup>57</sup>). In this series is a case in which it was apparently the cause of severe headache and this has been reported by others (Pringle<sup>107</sup>). The principal objection is that it is an unnecessary foreign body. Further, it would seem that there are other foreign bodies that are better tolerated, such as gold (Eston<sup>36</sup>), and which do not have the drawbacks of celluloid.

An attempt to evaluate the results of cranioplasty insofar as the symptoms of the patients are concerned is very difficult. The majority of the authors made no mention of the symptoms. From the cases that were adequately followed and reported, we find that Stieda,<sup>122</sup> out of eight cases, had two with occasional headaches, and one with vertigo and neuralgia of the supra-orbital nerve. Auvray<sup>1</sup> reported one case that had headache and epilepsy five months after operation. This case was reoperated upon by Villandre, and a ridge of cartilage was found pressing on the brain.

Boinet<sup>11</sup> reviewed 41 cases of cranioplasty and 95 cases of cranial defect that had not been repaired and found that there were no significant differences between the symptomatology of the cases whose defect had been filled and those in whom it was still open. It is, however, difficult to evaluate his figures accurately.

Marie,<sup>82</sup> in 1914, gave the details on 22 cases, six of whom were free of their symptoms or very much improved, 12 unchanged, and the remainder worse.

Primrose<sup>106</sup> reviewed 42 cases, 19 of whom were cured of their complaints, eight improved, five unchanged, and two made worse. Shuttleworth<sup>116</sup> reported seven cases, four of whom were relieved of their complaints and two improved, while one was the same as before operation.

Termier<sup>124</sup> was able to follow either personally or by letter some 63 cases that had been done 25 years before. He felt that only a few epileptics or

psychotic patients had been improved, but that the majority of the trephine syndromes had been cured or greatly benefited. Fourmestraux<sup>38</sup> followed 15 cases for ten years. Eight were well and had no complaints; seven still had some complaints of greater or less severity.

One of the most interesting and at the same time most important features that enter into this problem is the effect of cranioplasty on convulsive states. It has been variously reported by König,<sup>68</sup> who had a cure following cranioplasty; von Eiselberg,<sup>33</sup> who had three cases that were better up to three years after the operation; Stieda,<sup>122</sup> who had one cure and one unchanged; Mayet,<sup>86</sup> who had one cure; Chutro,<sup>22</sup> who reported one case cured and one improved; Boinet,<sup>12</sup> who had four cases improved and three unchanged; and Drevermann,<sup>32</sup> who had five cures and one improved out of 13 cases. Sudhoff<sup>123</sup> reported three cases that had epilepsy after but not before the operation. There have not been sufficiently accurate surveys to enable one to judge exactly the results of the operation. However, the majority of authors who have made any reference to epilepsy have reported that a certain number were either entirely relieved or improved. The cause of this and the mechanism behind it are not clear. Why, if a patient has convulsions following a cranial injury, does a repair of the cranial defect improve the convulsive state that must of necessity be due to the effect of the injury on the brain proper and not its coverings? The answer that immediately presents itself is that there is traction exerted on the brain by the overlying scar. And it is perfectly true that following a cranioplastic repair the dura probably assumes a more normal position. It is still hard to see just how this helps a condition caused by cerebral cicatrix. The fact, however, remains that a small but very definite percentage of these cases are relieved of their convulsions following cranioplasty.

From 1911 to 1938, 89 operations directed toward the repair of cranial defects have been performed at the Hospital of the University of Pennsylvania, and at the Graduate Hospital of the University of Pennsylvania. In an attempt to evaluate cranioplasty and learn how much benefit may be derived from it, we have reviewed these 83 cases. Adequate follow-up examinations have been obtained in 58. In 25, roentgenologic examinations were made showing the conditions of the grafts at periods up to 19 years following operation. The follow-up examinations were, with very few exceptions, made by ourselves and most of the roentgenologic studies were made under the direction of the Roentgenologic Department of the University Hospital.

*Indications.*—We were surprised to learn in going over the cases that the most frequent complaint was convulsive attacks. The other complaints in the order of their frequency are detailed in Table I.

It is often impossible to tell from the history the chief complaint of each patient and, therefore, just what was the indication for cranioplasty in each case. However, from the extensive histories of recent years, we feel that the syndrome of the trephined has not been a frequent indication for operation in either the early or later cases. All of these patients had cranial defects. It is surprising that only 13 came in for operation because of this alone.



TABLE I  
SYMPTOMS

Convulsive state.....	54
Grand mal.....	24
Focal attacks.....	27
Petit mal (including "unconscious spells").....	3
Defect without other symptoms.....	13
Weakness or paralysis.....	13
Headache.....	12
Numbness and other sensory changes.....	11
Visual disturbances.....	9
Field defects.....	3
Blurring or diplopia.....	6
Mental changes.....	4
Speech disturbances.....	3
Painful or pulsating scar.....	4
	<hr/> 123

The procedure that has been used in this clinic, almost to the exclusion of others, is a modification of the König-Müller operation that was developed by Dr. C. H. Frazier in the early nineteen hundreds and has been used here practically unchanged since that time.

TABLE II  
TYPES OF CRANIOPLASTY

Osteoperiosteal graft from the outer table of the skull.....	75
Split rib graft with or without periosteum.....	7
Celluloid.....	2
Fascia only.....	2
Osteoperiosteal graft from the tibia.....	1
Osteoperiosteal graft from the scapula.....	1
Split bone flap.....	1
	<hr/> 89

*Operative Procedure.*—After the skin and galea are reflected to expose the defect, the pericranium is freed from its edge. The pericranium should be carefully preserved. The dura is then freed from the under surface of the bone. The edge is trimmed back with a chisel until healthy, oozing bone is encountered. The upper surface is beveled outward leaving a broad bearing surface for the graft to lie upon, and during the chiseling the contour of the defect is rounded out as much as possible. A pattern of this defect is now made of rubber tissue or any other suitable material. This pattern should be one-quarter of an inch larger than the defect all around. The skin incision is now extended or a new incision is made to expose an area of the skull where thick bone is usually found, such as the parietal eminence or the occipital region, and the pattern laid out here. The pericranium is cut around the pattern with a scalpel and along this line a groove in the bone is chiseled (Fig. 1). Now, directing the chisel in this groove, nearly parallel to the surface of the

## REPAIR OF CRANIAL DEFECTS

bone, the outer table is gradually cut through to the diploe and then by chiseling through this, the graft is finally cut free. Care must be taken not to go through the inner table or another defect will be made. If this is done, and it is occasionally impossible not to do it, the small defect should be filled with little bone chips. The thin graft is now taken and molded so that the pericranial side is convex instead of concave, as it is when removed. The graft is then fitted into the defect and the periosteum of the graft is tightly sutured to the periosteum surrounding the defect with interrupted sutures (Fig. 2). The graft should have been cut large enough so that there is a good area of bone approximation all around; otherwise the periosteum will become adherent to the dura and form a barrier to new bone formation between the

FIG. 1

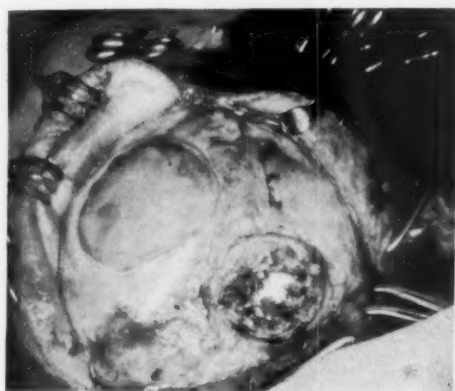
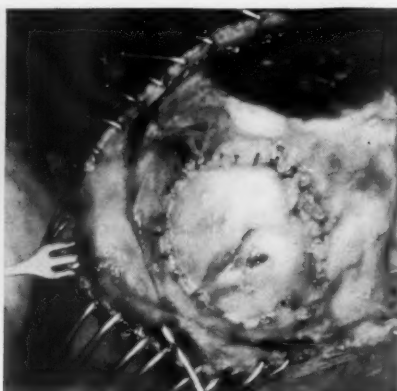


FIG. 2



FIGS. 1 and 2.—The defect has been exposed, and its edges freed from the pericranium and refreshed. A pattern of the defect is laid on an adjacent area of the skull, and the outer table, with its attached pericranium, is removed. The graft is then placed into the defect and the pericranium of the graft is sutured to the pericranium about the edges of the defect.

graft and the margin of the defect. The skin is closed with interrupted sutures in layers and drained for 24 hours.

When the defect is larger than 6x6 cm., a split rib graft is the most satisfactory procedure. The ribs are exposed in the posterior axillary line. After the periosteum has been elevated, a piece of the proper length is resected. The ninth and tenth ribs suit the purpose very nicely. The ribs are then split by hand with a sharp, thin chisel so that two pieces, one concave and the other convex toward the cut surface, are available. These are placed in warm saline while the defect is exposed. This is done as for the other type of graft until the bone edge is trimmed. When using ribs the defect is shaped into a triangle or quadrilateral and a groove is cut in two opposing sides into which the ends of the ribs may rest and be secured. The pieces of rib are now fitted accurately into the prepared grooves and cut to fit snugly side by side regardless of whether the cut or smooth surface is uppermost. When the pieces are in place, the edge is marked and the grafts removed while holes are bored in the margin of the defect and in the ends of the ribs. Stainless steel sutures are put through these holes and the ribs wired in position. If there is any

play between the central parts of the ribs, more steel sutures are placed from rib to rib. The pericranium is now drawn up over the edges of the grafts as far as possible and tacked there with silk sutures. The galea and skin are closed with interrupted silk, as usual, and the wound is drained only if necessary. It has been our custom to aspirate any collection from under the skin flap, thus avoiding drainage whenever possible.

The technics for the use of tibia, scapula, fascia and celluloid have been adequately described in the literature. We have not had enough experience with these types of repair to offer an opinion relative to them.

FIG. 3

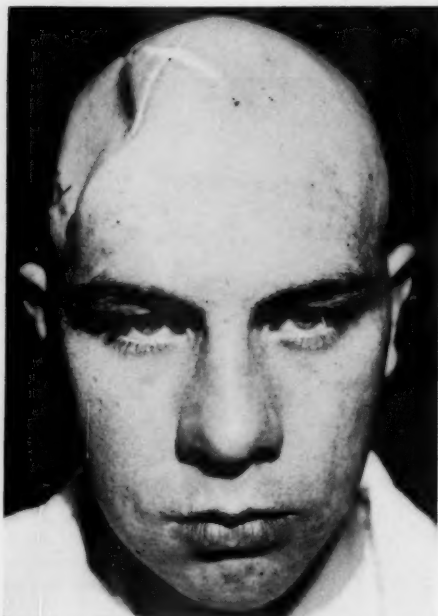


FIG. 4



FIGS. 3 and 4.—Showing a patient before and after repair of a cranial defect.

Patients are kept in bed for from five to seven days and are discharged in a week or ten days (Figs. 3 and 4). The average stay in hospital of simple cranioplasty cases during the last seven years has been  $14\frac{1}{2}$  days.

*Results.*—In the series of 83 cases having 89 operations, there were four postoperative deaths. Three of these cases had cortical excisions as well as cranioplasty, and the lateral ventricle was opened in two of them. The death following a simple cranioplasty was caused by postoperative meningitis. Of the other three cases, two died from infection and one from bronchopneumonia.

In addition to the simple cranioplasty, 14 cases had further surgical procedures directed toward the removal of bullets, excision of meningocerebral cicatrices, and the excision of a porencephalic cyst. For this reason these cases have been separated in evaluating the results from those having a simple cranioplasty.

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Postoperative complications were seen in 15 patients (Table III). Only three of these cases were badly enough infected so that at least a part of the graft was lost or absorbed. The others recovered promptly.

TABLE III

### POSTOPERATIVE COMPLICATIONS

Total cases.....	83
Deaths.....	4
Simple cranioplasty (infection).....	
Cranioplasty and cortical excision.....	3
(2 infections, 1 bronchopneumonia).....	1
Infections.....	8
With loss of graft.....	1
With loss of part of graft.....	1
With absorption of graft later.....	1
Outcome unknown.....	1
Superficial infections, grafts O. K.....	4
Delayed healing.....	5
With serous drainage.....	3
With hematoma.....	1
Unknown cause.....	1
Pneumothorax.....	2
Total.....	15

In the 58 cases that have been followed or examined, 48 show a satisfactory result as far as the plastic repair is concerned, from nine months to 19 years after operation. In a few cases there is a small depressed area in the center of the graft that does not pulsate, which in no way affects the efficiency of the graft, and does not give any trouble to the patient. Table IV summarizes the ten cases that are not considered satisfactory. Two cases show a small defect in the region from which the graft was taken. These defects are less than 1 cm. in diameter and cause no symptoms.

TABLE IV

### UNSATISFACTORY RESULTS OF 58 CASES FOLLOWED 9 MONTHS TO 19 YEARS

Absorption of graft.....	3
Depressed but solid.....	2
Graft depressible celluloid.....	2
(1 removed at later operation).....	
Loss of graft following infection.....	3
(1 has a satisfactory fascial repair).....	
Total.....	10

In seven patients with grafts from the outer table, a subsequent operation was carried out that exposed the inner surface of the graft. One case was operated upon by Dr. Ira Cohen, of New York, to whom we are indebted for the following information: "The graft was well healed and solid. The inner surface was rough, extended below the surface of the surrounding inner table

and was adherent to the dura and through it to degenerated brain." (The patient had had a cortical excision at the time of the cranioplasty.) The graft was removed in the hope that the release of the pressure would benefit his condition. Six cases that were reoperated upon in our clinic (Figs. 5, 6, 7 and 8), from one month to three years after cranioplasty, showed solidly healed grafts with irregular inner surfaces that projected very little beyond the inner surface of the skull. The graft was adherent to the dura in all cases but was easily freed, and no note was made of there being any adhesions through to

FIG. 5

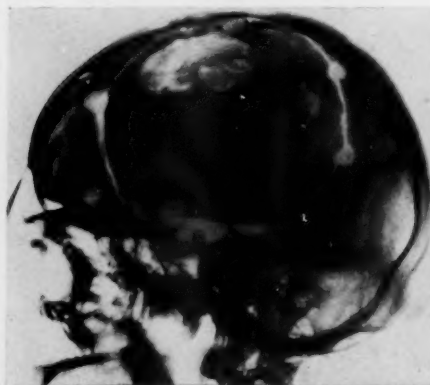


FIG. 6

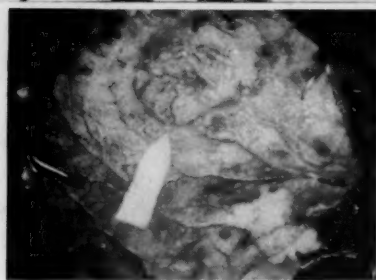


FIG. 7



FIG. 8

FIGS. 5, 6, 7 and 8.—In these two instances a bone flap was thrown about the repaired defect one year after cranioplasty had been performed. Note that in spite of an area of decreased density, suggesting absorption of graft, the operative picture of the inside of the bone flap shows that the graft is entirely healed in and solid.

the cerebrum. In one case, there was a small area not covered in by bone where the pericranium had become adherent to the dura. We feel that this case is important as it shows how a graft that is not approximated accurately might be unsatisfactory.

In one case of a celluloid cranioplasty, the graft was removed because of severe and prolonged headache. The celluloid was found to be enclosed in a sac formed by the pericranium and a bloodless, glistening membrane adherent to both pericranium and dura. This membrane was several millimeters thick and was intimately connected with the dura from which it was peeled off in layers like an onion until healthy dura was reached. The defect was repaired



## REPAIR OF CRANIAL DEFECTS

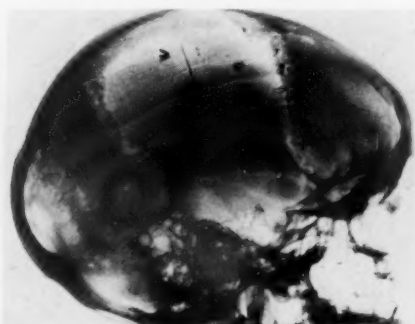
with split ribs. Examination two months later showed that the patient had been free from headache since the fifth postoperative day (Figs. 9 and 10).

Roentgenograms of grafts from the ninth month to the nineteenth year after

FIG. 9



FIG. 10



FIGS. 9 and 10.—Operative photograph and postoperative roentgenogram of a defect repaired by use of split rib graft.

FIG. 11

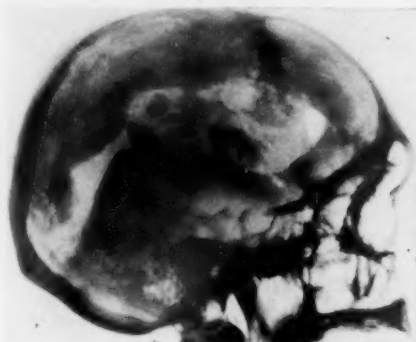


FIG. 12

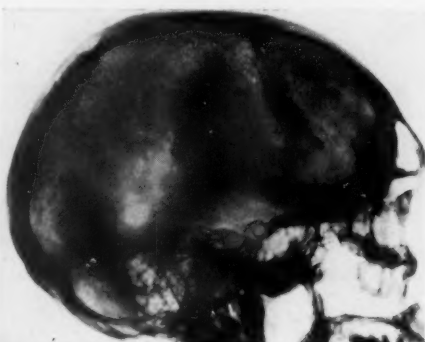


FIG. 13

FIGS. 11, 12 and 13.—Roentgenograms of repaired cranial defects 19 years (a), 11 years (b), and six years (c) after operation. In spite of presence of apparent defect in the cranial vault, the skull in each instance was entirely solid to palpation, no pulsation could be seen and no posttraumatic clinical symptoms were present.

the operation yield a good deal of information (Figs. 11, 12 and 13). One of the largest defects repaired by a graft from the outer table measured 6x13 cm. at operation. Figure 11 shows the roentgenographic appearance 19 years

later. There are many islands of bone in an area that is less dense and which might be a defect as far as one can tell from the roentgenogram. Examination of the area, however, shows it to be apparently solid bone without soft spots. The surface is irregular. The site of the removal of the graft is still visible in the roentgenograms but this too is solid to the examining finger. The appearance is rather typical of those found in other large defects. There appears to be a great difference in the thickness of the grafted bone or the new bone regenerated at the site of the graft.

This variability in the roentgenograms made their evaluation difficult. A local examination must be made at the same time to give the true result.

Two features in the roentgenogram of moderate sized grafts are noteworthy. First, there is frequently a less dense crescent around part of the

FIG. 14

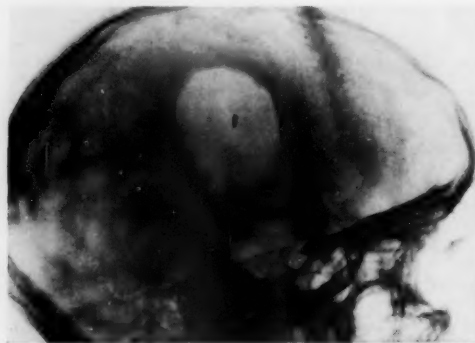
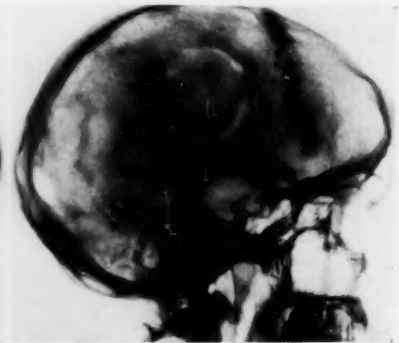


FIG. 15



FIGS. 14 and 15.—Cranial defect and cranioplasty six months after repair. Note the thin line of decreased density about the edge of graft, suggesting absorption. Graft entirely solid to palpation. No palpation could be seen or felt. Complete relief of clinical symptoms.

graft, that may or may not be ossified. Roentgenograms alone are unreliable and the area is too small to enable one to be sure from digital examination. Secondly, in some grafts the central portion is not as dense as the peripheral. This was true in the six cases that showed a small depression in the middle of the graft. In cases with this finding where a subsequent bone flap has been turned around the graft, no evidence of absorption of the graft has been seen. The graft seems to have healed readily into the surrounding bone.

A few generalities may be drawn from these roentgenologic studies: Healing in these grafts attains its maximum in less than a year, and thereafter little if any change can be demonstrated. In general it may be said that grafts in the frontal region will not bring about as thick a repair of bone as those in the posterior part of the skull. None of the grafts have shown any evidence of diploic formation, and the grafts are for the most part thinner than the surrounding skull. The site of the removal of the graft remains visible for many years as a thinner area of bone.

Figures 14 and 15 show a patient who had a very satisfactory graft at the end of six months. Three months later the graft has for the most part absorbed and a pulsating defect is now present that is tenser than normal. The patient has intracranial hypertension from some, as yet unknown, cause.

# REPAIR OF CRANIAL DEFECTS

TABLE V

## SYMPTOMS FOLLOWING OPERATION

Cases with simple cranioplasty .....	58
Convulsive state	
Free of attacks for 8 mos., 2, 4, 16, 17, and 19 yrs.....	6
One to 3 during postoperative period, then none for 9 mos., 1, 2, 7, and 18 yrs.....	7
Attacks for 3 and 6 yrs, then free for 16 and 9 yrs.....	2
Recurrence following another injury 8 mos. and 3 yrs.....	2
Free for 2 yrs., then spontaneous recurrence.....	1 18
Same after 1, 1½, 4, 5, 14, and 17 yrs.....	7
Worse—died in status 2 yrs. after.....	2 9
Total.....	27

TABLE VI

## CASES WITH CRANIOPLASTY PLUS CEREBRAL EXCISION

Convulsive state	
Free of attacks for 1½ and 6 yrs.....	2
One convulsion in 3½ yrs.....	1
Better (attacks fewer and less severe) 1½, 1½, 2, 3, 6, 7, and 19 yrs.....	7 10
Same for ¾, 1, 1, 2½, 6, 7, and 18 yrs.....	7
Worse—died in status 6 mos. after.....	1 8
Total.....	18

TABLE VII

## SYMPTOMS

		Good	Same
Cosmetic result satisfactory.....	7	7	
Cosmetic result failure (9 mos.).....	1		1
Painful defect satisfactory (4 and 18 yrs.).....	2	2	
Pulsating defect satisfactory (9 mos.).....	1	1	
Headache completely relieved (2, 4, 7, 7 and 16 yrs.).....	5	7	3
Less severe and frequent (1 and 18 yrs.).....	2		
Same (1 yr.).....	2		
Worse (case with celluloid plate 6 yrs.).....	1		
Dizziness relieved completely (6 and 16 yrs.).....	2	2	
Same (1 yr.).....	1		1
Weakness and paralysis (all but 2 had cerebral operations).....		6	5
Nearly entirely relieved (7 yrs.).....	1		
Improved, strength and function (1½, 3, 3, 6 and 19 yrs.).....	5		
Same (1½, 1½, 2, 3, and 6 yrs.).....	5		
Visual disturbances. Field defects all the same (3 mos., 1½, 2, and 5 yrs.).....	4		4
Numbness worse (1½ yrs.).....	1		1
Mental changes same after 1 yr.....	2		2
Better after 1½ yrs.....	1	1	
Totals.....	43	26	17

## CONCLUSIONS

- (1) Simple cranioplasty has definite indications beyond the closure of a defect.
- (2) Epilepsy is benefited by cranioplasty.
- (3) The syndrome of the trephined is relieved in the large majority of cases.
- (4) The cosmetic results of cranioplasty are excellent.

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DISCUSSION.—DR. WILLIAM JASON MIXTER (Boston): I think the subject considered by Doctor Grant a very valuable one to have brought up to date at the present time, because the literature has been full of various articles covering parts of this material.

I should agree absolutely with his idea that the outer table graft is the

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graft of choice, where it can be used. It is interesting to examine one of these grafts later when one turns down a bone flap including the graft, and to see that the graft has definitely thickened in a year or two.

In speaking of the various foreign materials, I agree with what he says about celluloid. Celluloid frequently causes a definite reaction about it. I operated upon one case that had had a gold plate put in nearly 20 years before. It was very interesting to compare the result in that case with the celluloid cases which have been reexplored. The gold plate apparently had stimulated absolutely no tissue reaction about it.

There is one thing that Doctor Grant did not mention, although I know that he uses it, because I have seen his cases, and that is that these patients must have a firm, protective dressing outside, in order that the graft may not be knocked in accidentally while the patient is asleep, during the first few days or weeks after operation.

There is one other point, and that is that where a patient has a depressed fracture, instead of lifting the depressed fragments, it is sometimes easier to take out the whole depression and turn it over, using the curve of the depression to match the curve of the skull.

DR. HOWARD C. NAFFZIGER (San Francisco): The most interesting and surprising point in Doctor Grant's presentation is the very high percentage of cures or improvement in convulsive states after simple repair of the bony defect, without resection of the brain scar. I had no idea that it would be so high.

We have performed many cranioplasties of the type that Doctor Grant recommends. It has certain obvious advantages, particularly in having only one field of operation exposed. Although I am unable to give our statistics, we have been disappointed by having the graft absorbed in a larger percentage of cases than he has, I am sure. That does not mean, necessarily, that the defect is as unprotected as it was before, because even in those instances in which absorption occurred, the defect was filled in by a heavy fibrous covering that gave adequate protection.

We have not been pleased with the results obtained by using foreign materials. There is one form of graft that we feel gives better cosmetic results than others and which we like for that reason. We have used it only recently. In one patient it was necessary to sacrifice a bone flap in the frontal area because of a meningioma which had invaded the sinuses extensively. We were anxious to secure a particularly good cosmetic result and, as one of our orthopedic associates is particularly skillful in removing grafts from the pelvis, we used grafts from the innominate bone. These can be chosen with reference to their curvature and can be removed with saw and chisel. They can be perfectly adapted in size and shape and give a better cosmetic result than any other type.

I think that possibly I have been a little prejudiced against extensive removals of bone from the skull by chisel, because of the necessity for the use of the hammer and the jarring it produces.

Any of the autografts may absorb. I had the opportunity of following the course of one patient for 22 years—from 1915 to 1937. A tremendous loss of bone from the frontal area was repaired with strips of osteoperiosteal grafts from the tibia, which gave an excellent cosmetic result. In roentgenograms, the grafts seemed to be unchanged for some five or six years, and then successive films showed that the strips of bone were becoming less and less dense and finally, at the end of something over 20 years, they could no longer be seen; the cosmetic result, however, was almost as satisfactory as in the beginning. The graft seemed to have been replaced by a very heavy fibrous covering.

DR. FRANCIS C. GRANT (closing): I am glad Doctor Mixter brought up the point of the postoperative protective dressing. I think it is very important. We incorporate a lead plate inside the bandage of sufficient size to overlap the defect, and that certainly prevents difficulty during the ten days the patient remains in the hospital, and after their discharge we fit them out with an aluminum protector which they wear for three months. That goes around the head and has a rubber band on it which holds it in place; and they are supposed to wear that pretty constantly during the next three months.

I was interested in what Doctor Naffziger said about the innominate bone. We have not used that. I do not see why it would not be a thoroughly satisfactory method for repairing a cranial defect.

As far as the gradual absorption of bone is concerned, I feel quite certain that that occurs, although we base that particularly on the roentgenologic appearance; and, when we studied these patients later, by actual palpation, and examination of the graft, it was amazing the way in which the roentgenograms had overestimated the condition of the graft. Those grafts are really in first-class shape. You could tap on them with your knuckle, and apparently they are just as hard as any other part of the patient's head, although roentgenologically they certainly looked as though a great amount of absorption had occurred.

We have been thoroughly satisfied with this procedure, and I see no reason from this study to change our opinion about it.



## EXPERIENCES WITH THE TOTAL AND INTRACAPSULAR EXTIRPATION OF ACOUSTIC NEUROMATA\*

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THE LIFE HISTORIES of many individual types of brain tumor, some of which are situated in a specific and well-known region of the intracranial cavity, have been worked out during the past quarter of a century, during which neurologic surgery has made such significant advances. It is now possible before operation not only frequently to recognize what type of growth one is dealing with, together with its exact situation, but also to predict with a fair degree of accuracy what the operative dangers will be as well as the future life expectancy and usefulness of the patient. Among the intracranial tumors to which these statements apply, the acoustic neuromata (the common cerebellopontile angle tumors) should probably be given the first place. The story of their recognition and the early surgical attacks upon them, their persistent resistance to complete extirpative methods, and their final capitulation, forms a long, but fascinating, although at times gruesome, chronicle in the annals of surgical advance.

It is not pertinent to the subject of this paper to retell this story which has been related so well by others, notably Cushing<sup>1</sup> and Dandy.<sup>2</sup> A few of the outstanding milestones, however, must be noted in order to get a proper background, and, therefore, some understanding of the difficulties pertaining to the enucleation of these growths, which, though entirely benign and encapsulated, are, nevertheless, so hemmed in by vital structures that their removal is attended with the greatest hazard.

Descriptions of the pathology of acoustic tumors go back to the latter part of the eighteenth century, and scattered clinical records are to be found through the early part of the nineteenth, notably that of Cruveilhier.<sup>3</sup> Their localization and clinical recognition had become fairly well established during the early years of the present century, following the advances made in cerebral and cerebellar localization.

Along with the earliest clinical localizations came an occasional surgical attempt at removal of these tumors, with a still more occasional successful result. Indeed, it is a matter of considerable wonder that any patient should have survived the operation as carried out at that time, namely, a quick, finger enucleation of the tumor with inevitable severe trauma to the brain stem and to the many cranial nerves and large blood vessels in the region. It must be borne in mind, however, that surgeons in that era were just beginning to acquire a knowledge of how to attack lesions of the brain and spinal cord and had

\* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

none of the modern adjuncts which we now regard as absolutely essential for this branch of surgery.

It is not surprising, therefore, that when the operative statistics concerning acoustic neuromata were brought to light at the International Congress of Medicine in London, in 1913, the mortality was so prohibitive as to make surgery seem well-nigh hopeless. Tooth's<sup>4</sup> report from the National Hospital at Queen Square, London, showed a 58 per cent mortality in the cases presumably operated upon by Sir Victor Horsley, and of the 12 patients it is probable that only one of the five survivors may have had a complete extirpation. The story from continental Europe at the same Congress was even worse, von Eiselsberg reporting 12 deaths in 16 cases, an operative mortality of 75 per cent, and Krause 26 deaths in 31 cases, an 83.8 per cent mortality rate. From both of these series it is fair to assume from the records that only one (a patient of von Eiselsberg's) survived for any prolonged useful period.

The first notable advance from this desperate situation in the surgical treatment of acoustic tumors came with the publication, in 1917, of Cushing's monograph on Tumors of the Nervous Acousticus.<sup>1</sup> In this work the method of intracapsular enucleation of the tumor was described, and although admittedly not an ideal operation for a benign, encapsulated lesion, nevertheless a patient was, for the first time, offered a procedure which carried a relatively low mortality (20 per cent at that time); relief from pressure symptoms and, not infrequently, rehabilitation to useful life for perhaps two to eight years. In a subsequent publication,<sup>5</sup> in 1932, Cushing reviewed his later experiences with acoustic tumors showing that the mortality had been reduced to 4 per cent in his last 50 cases. It was later brought out by Eisenhardt,<sup>6</sup> in looking up the patients in Doctor Cushing's series who had survived five years or longer, that 77 cases of acoustic neuromata fell within this category, and of these, 63 were still living from five to 26 years—a record which has not been approached for this type of operation by any other neurosurgeon. Mere survival, however, does not tell the whole story although in this instance it was an enormous stride ahead in the treatment of these growths. Possibly a better idea as to what could be expected from a radical intracapsular enucleation was reported by Cairns<sup>7</sup> in reviewing the condition of the patients he had seen on Doctor Cushing's service after an interval of nine years. There were ten cases of acoustic tumor in this series and of this number there were eight survivors. Of these, three were at work, three were severely incapacitated and two had considerable disturbance of gait. Van Wagenen,<sup>8</sup> in 1934, made a similar follow-up study of a series of Doctor Cushing's cases after an eight-year interval. Of the 11 acoustic tumor patients, seven were living, and of these, four were "in excellent condition and able to go about their usual duties." The other three were up and about although two had been blind before operation and had remained so.

The second great step toward a more permanently satisfactory operation for acoustic neuromata was furnished by Dandy,<sup>9</sup> who, in 1922, outlined a method for the total extirpation of these tumors, and, in 1925, reported<sup>2</sup> five

successful total extirpations. The mortality for this operation given by Dandy, in 1932,<sup>10</sup> was 20 per cent. Recently (1934), Olivecrona<sup>11</sup> of Stockholm has likewise advocated total removal of acoustic tumors by Dandy's method, and in 31 cases his mortality was 19.4 per cent.

The operative method offered by Dandy, briefly, is as follows: He at first employed a bilateral cerebellar exposure, but more recently<sup>12</sup> (1934) he has advocated a unilateral approach. After tapping the lateral ventricle and evacuating as much fluid as possible from the cisterna magna, the outer third of the cerebellar hemisphere is excised, giving an excellent exposure of the growth in the cerebellopontile angle. This important step in the technic was used for better exposure of these tumors in the majority of his cases by Cushing<sup>5</sup> since 1928. The capsule of the tumor is now incised and its contents carefully removed with a curet. Following this the capsule is grasped with forceps and drawn away from the brain stem, clipping such vessels as may be encountered. The tumor is carefully separated from the fifth nerve above and from the ninth, tenth and eleventh nerves below. Finally its attachment at the internal auditory meatus is divided, the tumor removed and the meatus cleaned out.

The advantages of complete removal contrasted with even a painstaking intracapsular extirpation of acoustic tumors must be obvious. The surviving patients in almost every instance are enabled to return to their former activities, presumably without fear of a recurrence of their tumor. The chief disadvantage of the complete operation is the facial paralysis on the side of the lesion, but this can be greatly benefited by a spinofacial or hypoglossofacial anastomosis.

In favor of the intracapsular method, one can only say that there is almost never any facial palsy and that the initial mortality, up to the present time, has been about half that of the complete operation in such series as have been reported. Against these factors, however, are inevitable recurrence, leading either to a further serious operation or to death, and, thus, a far greater eventual mortality than when the tumors are primarily completely removed. In addition, the chances of a patient getting back to useful work after the intracapsular operation are not nearly so great as when the tumor is taken out totally.

Nevertheless, there may still be instances in which the less hazardous operation, with sparing of the facial nerve, is indicated, although in our own experience total removal of all acoustic tumors previously unoperated upon has been performed without exception during the last four years. Patients are always informed about the resulting facial paralysis, and only one has declined for this reason and had the intracapsular operation elsewhere. Without all the adjuncts of modern neurosurgery, however, including a highly trained team, adequate suction and a good electrosurgical unit, it is doubtful whether complete extirpation should ever be attempted.

*Operative Procedure.*—The operation which we use is similar to the pro-

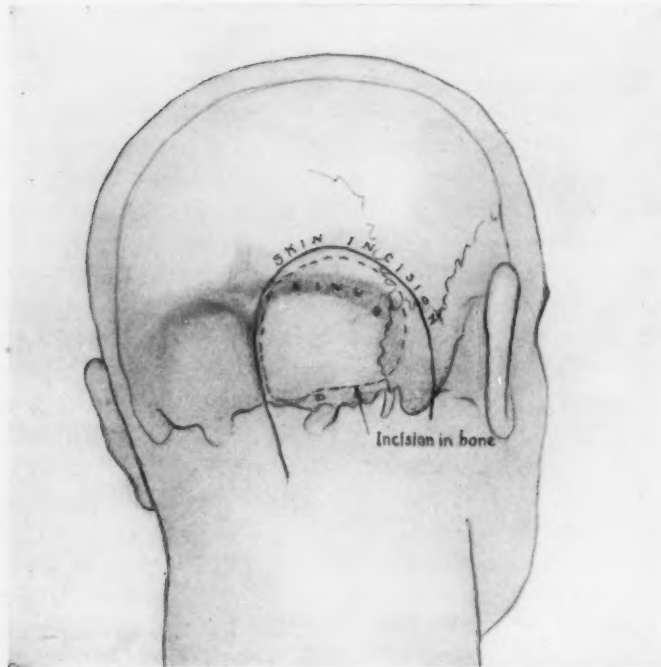


FIG. 1.—Outline of unilateral skin and muscle flap over the suboccipital region, showing its relation to the lateral sinus.

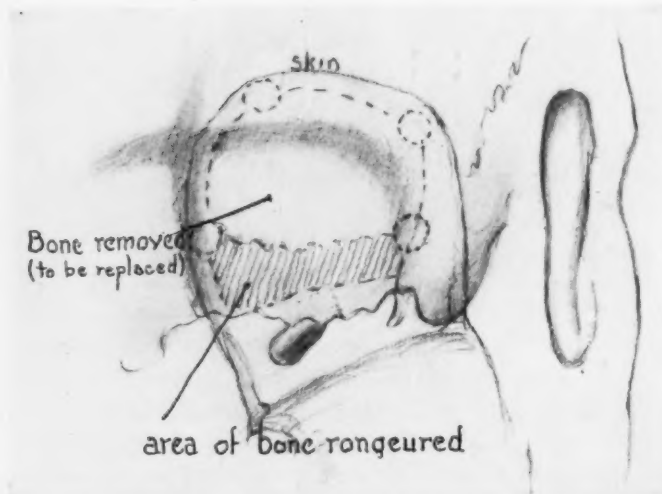


FIG. 2.—Area of bone removed *en bloc*, to be replaced at end of operation. The upper margin of bony opening is well above the lateral sinus. Further bone removed by rongeurs in lower portion of field for full exposure.

cedures described by Dandy and Olivecrona with certain modifications which we believe are important.

In the first place, a rather large unilateral skin and muscle flap is turned down over the suboccipital region on the side of the tumor (Fig. 1). Following this, a piece of bone is taken out by the use of bur holes connected with the Gigli saw, going well above the lateral sinus (Fig. 2). This bone is replaced at the end of the operation. Further bone is removed by the rongeur at the lower margin of the area. The dura is next opened to the limits of the bony opening, except superiorly where it is incised up to the edge of sinus. This permits exposure directly down the tentorium. The outer third of cerebellum is always uncapped, after which the lateral aspect of tumor is fully exposed in the angle. From this point our procedure is almost identical with Dandy's. The capsule of growth is incised, and its contents evacuated as thoroughly as possible, great care being taken not to get through the capsule medially (Fig. 3). Some tumors are highly vascular, and bleeding from the interior has to be controlled by pressure with cotton moistened in saline or sometimes a little Zenker's

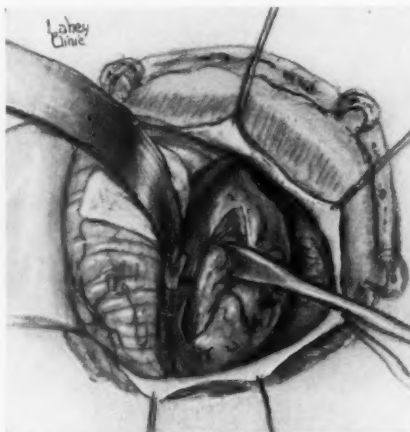


FIG. 3.—Outer third of cerebellar hemisphere "uncapped." Tumor exposed in the angle. Preliminary excavation with curet.

solution may be used on cotton. Likewise the capsules of different tumors vary greatly in their toughness, but most of them can be grasped and drawn gently away from the cerebellum and pons while strips of moist cotton are inserted as the entering vessels are clipped. It is usually fairly easy to separate the growth from the lower group of nerves (ninth, tenth and eleventh), but there is almost always a large branch from the vertebral artery at this lower pole and this must be ligated with silver clips (Fig. 4).

Separation of the tumor capsule from the fifth nerve is often difficult, due to great adherence, but as a rule it can be accomplished without too great contusion (Fig. 5). This is highly important, as the combination of facial paralysis together with facial anesthesia leads frequently to corneal complications. When the fifth nerve has been damaged, it is our custom to suture the outer portion of the eyelids to each other, thus giving the cornea almost complete protection.

When the tumor has been mobilized at its upper and lower poles, and partial separation from the pons has been accomplished, the tumor's attachment at the internal auditory meatus is divided by cutting and coagulation. This permits the final withdrawal of the capsule from the side of pons and medulla, thus completing the enucleation except for that portion of growth within the



meatus (Figs. 4 and 6). This is curetted out and coagulation applied. Often, too, it has been necessary to chip off the bony ridge over the meatus in order to expose it thoroughly and to be sure of getting tumor cells lying far within it.

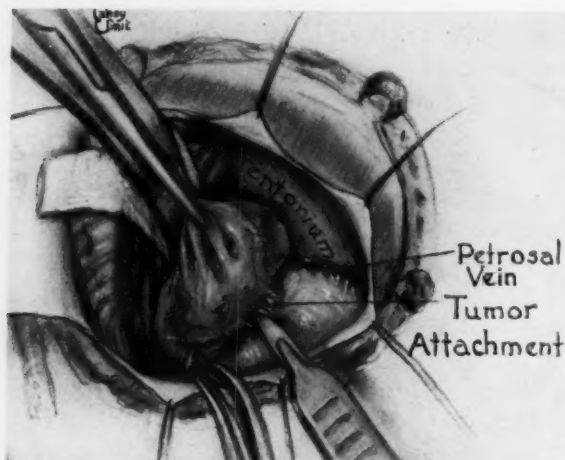


FIG. 4.—Tumor capsule grasped with forceps and lifted upward. Large artery at lower pole ligated with silver clip. Tumor attachment at internal auditory meatus divided with knife after coagulation.

The bed from which the tumor has been taken should be left completely dry, otherwise postoperative oozing will take place, a clot will form, and re-opening of the wound will be necessitated. After careful hemostasis the dura

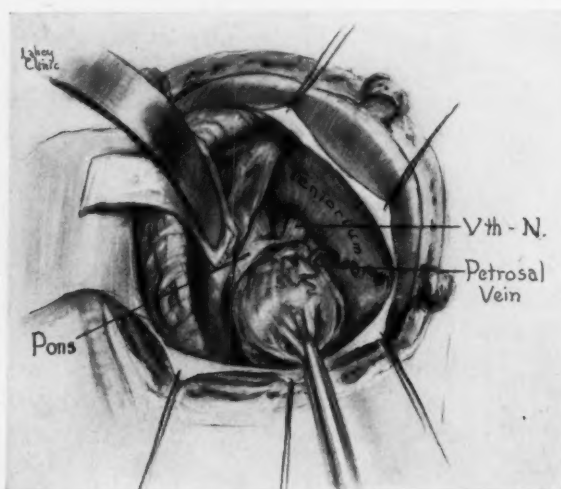


FIG. 5.—The tumor drawn downward and separated from the trigeminal nerve at its upper pole.

is resutured, the upper piece of bone replaced and the skin and muscle flap closed in layers with fine silk without drainage. While the convalescence of many of these patients is uneventful they must all be watched carefully, par-

ticularly for difficulty in swallowing and inability to get rid of mucus secretion in the throat. Such secretion should be sucked out promptly by using a fairly small catheter attached to a suction apparatus, passing the catheter either via the nares or the mouth. Nasal feeding is carried out until the patient can swallow well without choking.

*Correction of Facial Paralysis.*—Any time after a two weeks' interval a spinofacial anastomosis is made. In our experience, this is preferable to using the hypoglossal nerve unless the spinal accessory has been injured. Such an

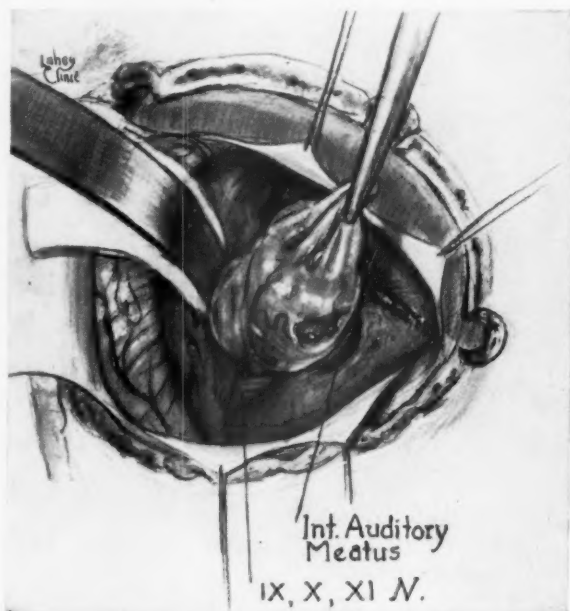


FIG. 6.—Final mobilization of tumor after its attachment has been divided. The ninth, tenth and eleventh nerves are seen as a group under the tumor's lower pole.

anastomosis gives reasonably good facial function within about a year (Fig. 7). In one patient, the facial nerve was preserved at operation, although in this instance it is possible that a few cells may have been left within the meatus (Fig. 8). A similar episode was reported by Cairns<sup>13</sup> in 1931.

*Material, Statistics and Results.*—In the present study there are included all cases of verified acoustic tumors seen since the organization of the Neurosurgical Service at the Lahey Clinic, November 1, 1932 (six and one-half years ago). There have been 35 patients in all, but for obvious reasons they must be divided into two groups, namely, those not having been operated upon previously, 23 in number (Group I), and the recurrent cases, of which there were 12, all of whom had had one or more previous intracapsular partial extirpations (Group II). The reason for this division is because the difficulties and dangers in the complete extirpation of recurrent tumors are infinitely greater than is the case with tumors which are exposed for the first time. In fact, Dandy<sup>10</sup> goes so far as to say that "... after one operation has been



FIG. 7.—(A) Patient with left facial paralysis after removal of acoustic tumor. (B) The same patient eight months after a spinofacial anastomosis showing ability to close left eye completely. (C) The same patient with face in repose after the anastomosis.

# ACOUSTIC NEUROMATA

performed, the adhesions are so great that careful dissection of the tumor at a later date is practically impossible." Therefore, a fair comparison of our series with those of others is possible only when the number of primary and



FIG. 8.—Patient whose facial nerve was spared at operation. (A) Slight left facial weakness three weeks postoperative. (B) The same patient two years later.

recurrent cases, with their respective data, is known. This may be given in the following summaries:

TABLE I

## CASES PREVIOUSLY UNOPERATED UPON

Group I. Cases previously unoperated upon.....	23
Intracapsular removal.....	3
First stage suboccipital decompression.....	1
(No deaths in hospital. All have died subsequently, 1 to 3 years; 3 from recurrence; 1 from intercurrent cause.)	
Complete removal.....	19
Deaths.....	2
Mortality.....	10.5%
Total operative mortality for Group I.....	8.7%

*Comment.*—There is little to be said concerning the patients in both groups who had incomplete intracapsular enucleations. There were only six in all, and the survivors, on the whole, did not do as well as had been expected. It was for this reason, doubtless, that we were led into attempting complete extirpations.

The 19 patients in Group I, who had their tumors totally removed, are perhaps of chief interest, since they were operated upon before previous surgical intervention, and, therefore, with a few exceptions, had not suffered severe

brain stem or cranial nerve damage. Two of the patients in this group, unfortunately, were blind before they came for operation, a circumstance which is lamentable in the light of our present knowledge of the diagnosis and treatment of intracranial tumors.

There were two deaths among the 19 patients in this group; one from meningitis which developed 16 days postoperatively, presumably from an opened mastoid cell, and the other from pneumonia in a man who had not only the usual intracranial neuroma but also a large paravertebral extension of his tumor outside the spinal column in the upper cervical region. He was in extremely poor condition before operation.

The 17 surviving patients are all alive from two months to four years since their operations. All but two are either in good or excellent physical condition, able to get about perfectly well by themselves, and, for the most part, to resume their former occupations. This of course does not apply to the two patients who were blind before being operated upon. Three patients have had corneal complications because of damage to the fifth nerve, but none has had to have an eye removed. Several other patients have had a moderate degree of trigeminal hypesthesia, but sensation is sufficient to allow a corneal reflex. Nearly all the group have had spinofacial anastomoses by one of us (J. L. P.), so that their facial paralyses have been greatly benefited (*cf.* Fig. 7). The amount of ataxia and unsteadiness varies considerably in the different individuals, but tends to be minimal after the lapse of a year.

TABLE II

## CASES HAVING BEEN PREVIOUSLY OPERATED UPON

Group II. Recurrent cases.....	12
(Patients previously operated upon by us or elsewhere, intracapsular removal having been performed.)	
Further intracapsular removal.....	3
Deaths.....	2
Mortality.....	66.6%
Complete removal.....	9
Deaths.....	3
Mortality.....	33.3%
Total operative mortality for Group II.....	41.6%

In Group II, there were nine patients whose tumors were entirely extirpated. As intimated previously, the difficulty here was excessive, not only from adhesions to the brain stem but also because of the tremendous extension of the tumor—sometimes far beneath the pons to the opposite side, entirely covering the basilar artery and likewise extending upward into the incisura and downward into the foramen magnum. Three of the nine patients died—all from pulmonary complications due to difficulties in swallowing. The six living patients are all in surprisingly good condition considering their previous disability. Three have been able to resume their former occupations, and the other three are able to do work about the house although one has been nearly blind since the time of his first operation.



SUMMARY

The operative and end-results in a series of 35 patients with verified acoustic tumors are presented. Certain features of the operative technic for the total removal of these neuromata are given in detail. Since, in our hands, intracapsular removal of the tumors has been unsatisfactory and the eventual mortality extremely high, complete extirpation is now carried out on all cases, whether primary or recurrent. The operative as well as the total mortality for complete removal of tumors previously unoperated upon is 10.5 per cent. When this procedure has been carried out on recurrent tumors the mortality is 33.3 per cent. The combined mortality for both primary and recurrent tumors totally extirpated is 17.8 per cent.

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DISCUSSION.—DR. MAX M. PEET (Ann Arbor, Mich.): We have used a unilateral approach for acoustic tumors during the last ten or 12 years, and it certainly has many advantages. We have also been performing as complete as intracapsular excision as possible and then pulling the capsule out—in other words, complete extirpation of the tumor. We felt that this was necessary for the same reason that Doctor Horrax does. Some patients had remarkably rapid recurrence. One such patient Doctor Horrax happened to see me operate upon. I had taken out the whole tumor, including all the capsule except that portion extending into the internal auditory meatus. I wanted to save the facial nerve, and I had succeeded in saving it up to that point, and so we left a small amount of tumor inside the internal auditory meatus. Within six months his symptoms had all returned, and at operation I found the tumor just as large as the original one. In fact, the gross appearance did not seem

to be much different. At the second operation I took out the whole tumor and then thoroughly cauterized, using the Bovie unit, everything within the internal auditory meatus. I think we are justified in producing a facial paralysis in all these individuals. It can be corrected by a spinofacial anastomosis. The latter preserves the tone of the face and the patients can smile voluntarily. I admit they do not smile involuntarily. If they want to make a good appearance, they have to think about smiling, but that is infinitely better than having a recurrence, as some patients do in a comparatively short time.

I think the actual mortality for complete excision of acoustic tumors by the technic Doctor Horrax has shown, is no greater than the partial operation which has been performed so many times before, and the final results, so far as the patient is concerned, are infinitely better.

DR. FREDERICK L. REICHERT (San Francisco): The discontinuance of the whose exposure of the cerebellum and the use of the unilateral approach with a deliberate resection of the outer part of the cerebellar lobe has made a marked improvement in the operative removal of the acoustic tumors.

We have tried to save the facial nerve, which is a much tougher nerve than the eighth, and by carefully dissecting the capsule down to the seventh nerve and then coagulating it, we have been able, in the last few cases, to preserve the facial nerve. I think that is a procedure that might be tried in many of the cases.

DR. GILBERT HORRAX (closing): There was one thing which I neglected to mention, and that concerned the internal auditory meatus. We did save the patient's facial nerve in one instance, but in my experience, the tumors always extend well into the internal auditory meatus to quite a considerable depth and, therefore, if you are going to be sure of getting every cell out, you must deal with it in some way, and what I should have said was that we always curet the meatus, and not only that, but it has been found necessary, very usually, to either chip off the bony ridge over the meatus so that you can get at it better, or make some bur openings there with a small drill and take it off that way, lest you should break into the mastoid cells by chipping it off. Then we not only curet out the meatus, but also coagulate as far in as possible with some suitable instrument.

Now, it is true, as Doctor Reichert says, and as we have done once and as Dr. Hugh Cairns, of London, has done once, as doubtless others have, that we can save the facial nerve, but I am very sure in so doing we do leave some cells.

It is obvious that not all of these tumors are going to recur as rapidly as the one Doctor Peet has mentioned, because some of them have gone on for many years. On the other hand, I feel we are leaving a loophole for recurrence if we do spare the facial nerve, although one would always like to, so it is our custom, almost invariably, to curet out the meatus and cauterize it with the electrosurgical outfit so that we can be sure of not leaving any cells to recur.

## INTRACRANIAL ARTERIOVENOUS ANEURYSMS\*

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GALVESTON, TEX.

It is with an apology that I impose upon this Society a paper upon a subject which has been studied and analyzed so many times by those who have had more extensive and much more expert knowledge than I. Still, there is an unexplainable fascination about vascular disorders and they offer a real challenge, for the anatomy and circulation of the blood have not completely lost their mystery, though Harvey has been dead for nearly 300 years. The addition of four cases to the long list of intracranial arteriovenous aneurysms already reported is a small justification for the paper, and yet each one shows some points of interest, either in anatomy or in its response to treatment.

Because the larger arteries and veins within the skull do not parallel one another, fistulae, other than the congenital angioma where direct arteriovenous communications occur without capillaries intervening, are rare except for the carotid-cavernous sinus type, which may be congenital or more often traumatic in etiology. But, as has been frequently noted, because of the unusual anatomic situation of the carotid artery within the cavernous sinus before it reaches the brain, such fistulae are relatively common. The cirroid intracranial aneurysms, though less frequent, are often confused with the carotid-cavernous types. Two of the cases here reported are of this type and are of a serious nature. The problem of dealing with them is no less interesting than the two carotid-cavernous cases.

### CASE REPORTS

**Case 1.**—U. H. No. 24892: J. W. T., white, male, age seven, entered the John Sealy Hospital, May 17, 1928, giving the following history: Since birth the right side of the face had been of a darker color than the left and had appeared dusky and flushed at all times. The condition had grown steadily worse during the past few years.

*Physical Examination* revealed a well-nourished child, not acutely ill. The whole right side of the face, scalp, and upper part of the neck was dark and cyanotic in appearance. The superficial veins were engorged and could be seen pulsating. The condition was not that of a cavernous hemangioma since only the normal number of veins were present, although they were greatly engorged over the entire half of the face and head. The right eye showed a moderate proptosis with congestion of the conjunctiva. On auscultation, a loud bruit could be heard over the entire right side of the head, face, and neck. There was a fairly sharp line of demarcation between the two sides of the face. Pulse ranged from 110 to 120 at rest. The eye examination showed the retinal vessels congested, but vision was apparently not defective.

We considered this a congenital cirroid aneurysm after exploring the carotids and finding no fistula between the carotids and jugular vein, but the location of the cirroid aneurysm was never definite, and even now we are reluctant to predict its location. Still, there is a possibility that there may have been a carotid-cavernous aneurysm as well. The treatment was the same as if it had been such an aneurysm.

\* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

*Operation.*—May 17, 1928: The common, internal and external carotids were exposed on the right side. No fistula was found. The common carotid was occluded with a Halsted aluminum band. No cerebral symptoms developed, and following the operation there was much less engorgement of the veins of the face and eye; the murmur persisted, though it was much less pronounced.

On July 28, 1928, the patient was again admitted to the hospital. There was only slight improvement since the previous admission, and, according to the records, there was a very marked to-and-fro, swishing murmur audible over the right side of the face and head, much less marked on the left side. Vision in the right eye was markedly diminished, and the eye was prominent. It was thought that collateral circulation through the branches of the external carotid had restored the circulation.

*Second Operation.*—July 29, 1928: The right external carotid was exposed and ligated. It showed only slight bleeding when cut. The facial, lingual, occipital, and other



FIG. 1.—Case 1: Patient ten years after carotid occlusion for cirroid intracranial aneurysm resulting in hemiplegia.

branches were separately ligated. Following this operation the right side of the face was much less congested, and the murmur was much less pronounced, but to our surprise it now appeared louder on the left side of the face and neck. This change was difficult to explain. The patient went home on the fifth day, and on the ninth day after operation his mother noticed that his left hand, arm, and leg were partially paralyzed.

The patient was not seen again until March 1, 1939 (ten years later), at which time we found him a boy of 18 years, weighing 160 pounds. He was lame with the gait of the average long-standing hemiplegic. The left leg was smaller than the right and quite spastic, with exaggerated reflexes. The left arm was small, spastic, and underdeveloped. The face was not involved in the paralysis, but the right side of the face and head was much larger than the left (Fig. 1) and was of a dusky color due to the great engorgement of all the superficial veins. As on the first admission, the line of demarcation between the two sides of the face was sharply defined. The right eye was prominent, and the conjunctival veins were engorged. A systolic murmur was present over the head, face, and eyes, still much louder on the left, or unaffected side. The heart sounds were regular with a rate of 110 to 120. Compression of the right jugular increased the con-

gestion. Compression of the left carotid did not effect the murmur. Palpation on the right side of the skull revealed irregularities in the bone beneath the varicosed veins. Roentgenograms showed extensive calcification over the cortex of the brain on the right side with grooving of the skull in many pieces from the dilated scalp veins. Sight in the right eye was almost lost. Fingers could be counted by this eye, but nothing more. Vision in the left eye was corrected to good sight with glasses. The mentality of the boy was slightly below normal.

*Roentgenologic Study.*—"The teleroentgenogram shows quite an increase in the cardiac shadow, the percentage of increase at the apex being 16.3. Studies of the skull show an unusual type of calcification over the right half of the cranium extending from the frontal area posteriorly to the occipitoparietal region. The calcification appears to be within the skull, and is apparently in the meninges or the cortical area of the brain. Throughout this area one can see canalizations which give the impression of vascular channels, suggesting that this calcification might be an extensive hemangioma of the cranium in the right parietal area. There is marked thinning of the right temporal region. There is an irregular increase in the thickness of the skull. Irregular defects in the frontal area due to dilatation in the emissary channels. There is extreme dilatation of the diploic channels, especially in the right side."

*Discussion of Case 1.*—There is some question as to the correctness of our assumption that there was a carotid-cavernous sinus fistula in addition to the cavernous angioma, but because of the eye symptoms we could not ignore this possible conclusion.

Nine days following the internal carotid occlusion, this patient developed a hemiplegia. Whether this was due to cerebral anemia following ligation or the extension of a thrombosis to the circle of Willis, or due to an embolus dislodged from an old thrombosis resulting from the carotid ligation, we cannot say. It seems more logical to attribute the paralysis to the cause last mentioned. This complication might indicate that occlusion of the carotid in the young is not without danger, though not necessarily so. Another interesting observation was the shifting of the murmur to the left side of the head and neck following the occlusion of the carotids on the right side.

The results of the embolus were very deplorable. The cerebral accident was more distressing than the original affliction. The carotid occlusions had improved the condition only temporarily, and the location of the fistulae was still obscure. We surmised that they were intracranial and multiple. In the beginning we felt that there was an opening between the internal carotid and the jugular at the base of the skull. Though there was a great deal of back pressure in the ophthalmic veins of the right side, we could not be sure it was a carotid-cavernous fistula. At the present time the patient's parents will not agree to further treatment.

*Case 2.*—Hosp. No. 57334: Mrs. R., white, female, age 53, entered the hospital, January 21, 1938, complaining of a roaring in her head, headaches associated with vomiting, and a staggering gait. The symptoms had begun two years before, and during the past six months they had grown much worse, with the development of an ataxic gait. Three months previously, the patient had an unconscious spell and was in bed several weeks with dizziness. Neurologic and physical examination showed the patient to be a slight woman, undernourished and ill. The pupils were equal and reacted to light. The disks appeared normal. Ocular muscles were intact with some lateral nystagmus. There



was no facial weakness, but there was a marked cerebellar ataxia. Equilibrium was better on the right foot than on the left. There was ataxia on heel-to-knee test on both sides, more marked on the left. Motor power and muscle status were normal. There were no pathologic reflexes. There was only slight bone conduction of the left ear. The left fifth and eighth nerves were definitely involved, suggesting a posterior fossa lesion.

There was a visible pulsation of the vessels below the left ear and over the left mastoid area, and a palpable thrill was found in this region. A loud systolic murmur was heard over the entire head, loudest over the left mastoid region and less pronounced on the right. Compression of the right carotids did not influence the murmur, nor did compression of the left common carotid. But compression of the carotid on the left side at the bifurcation stopped the noise completely. The veins of the head were only slightly congested. Roentgenogram of the skull was negative. *Diagnosis:* Intracranial arterio-venous aneurysm of the cirroid type.

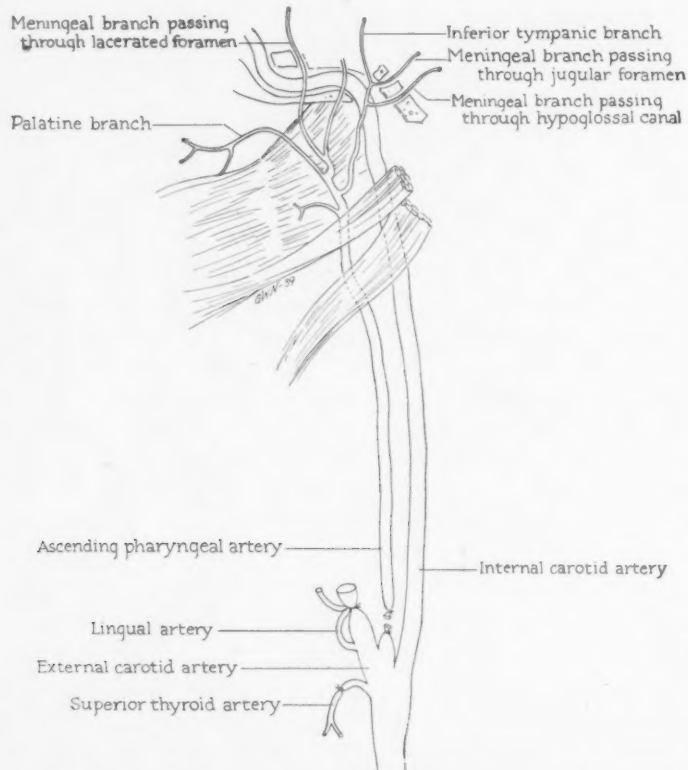


FIG. 2.—Case 2: Greatly enlarged ascending pharyngeal artery supplying chief circulation to intracranial cirroid aneurysm.

*Operation.*—February 1, 1938: The left carotid vessels were exposed under local anesthesia. Arising from the fork of the common carotid was an abnormally large vessel, evidently the ascending pharyngeal, which is ordinarily very small but here was half as large as the internal or external carotid (Fig. 2). It was thin-walled and more purplish in color than the large arteries. Compression of the common carotid did not affect the murmur, nor did compression of the internal and external separately. Occlusion of the ascending pharyngeal stopped the murmur. This vessel was cut between ligatures, and the external carotid was also ligated. Convalescence was uninterrupted, and the patient remained in bed for ten days. She was much better in every way; the

roaring in the head had gone; headache and vomiting and ataxia gait were greatly improved. She left the hospital, February 12, 1938.

The patient entered the hospital again on March 28, 1938. She was in good general condition, but there was nerve deafness in the left ear as before. There was no ataxia, and the patient heard the murmur only slightly, but the palpable pulsation had returned over the left mastoid area though it was less pronounced than previously. A bruit was heard over this area, more limited than before. The left superficial temporal artery was not palpable.

*Second Operation.*—March 29, 1938: A curved incision was made down to the skull over the mastoid region, surrounding the vascular area previously described, and the flap was turned up with all branches of the great auricular and occipital arteries severed and tied. The large emissary mastoid vein was ligated as it entered the skull. The result was a cessation of the murmur as well as the pulsation.

A follow-up in February, 1939, reported that the patient was comfortable, free from all symptoms except the left ear deafness and the presence of a faint bruit.

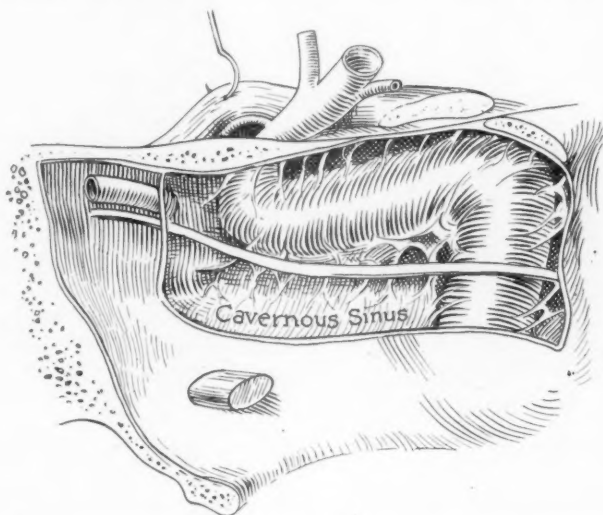


FIG. 3.—Internal carotid after passing through cavernous sinus (after Jackson).

*Discussion of Case 2.*—This case is of anatomic interest because of the part played by the ascending pharyngeal artery, which has assumed enormous proportions, though normally it is very small and insignificant. This artery passes upward, supplying branches to the pharyngeal-tympanic tube and palate, and its *inferior tympanic* branch accompanies the tympanic branch of the glossopharyngeal nerve to the tympanic cavity. It also gives off the posterior meningeal, branches of which enter the skull through the foramen lacerum, jugular foramen, and anterior condylar canal. The ligation of the ascending pharyngeal artery decreased the activity of the aneurysm. Though the murmur and thrill disappeared for some time, improvement was permanent only after destroying externally the communicating circulation through the cranial vessels over the mastoid and occipital regions, which was chiefly through the large emissary mastoid vein into the cranium.

Carotid-cavernous aneurysms have been given a most thorough study and

extensive discussion in medical literature, and still they have their hidden, unexplained problems. Locke collected from the literature 588 cases reported prior to 1923. Dorrance and Loudenslager reviewed 275 cases occurring between 1908 and 1934. These represent a small number of the cases actually occurring. The contributions of H. Sattler, deSchweinitz, C. H. Sattler, Matas, Locke, and more recently Dandy, should be carefully studied and restudied before one attempts to treat such an aneurysm. We offer very little new upon the subject, but submit the reports of two cases, some features of which are of interest as an anatomic study, as well as the results of the treatments employed.

**Case 3.**—U. H. No. 26069: M. R., Negro, female, age 39, entered the John Sealy Hospital, September 27, 1928. She was a well-nourished Negress, not acutely ill. She stated that for the past two months the right eye had been swelling at night and subsiding in the morning when she got up. She had had pain in the eye in addition to the swelling. One week following an attack of influenza she was awakened at night by a feeling as if "something turned loose inside her head and there was a noise in her right ear like a

train puffing and roaring." It seemed as if the sound came from under the pillow. From the time of onset this noise annoyed the patient constantly. It was somewhat worse at night.

*Physical Examination* revealed that the pupils were unequal (right Mm.; left 3.5 Mm.) but they reacted to light and accommodation. There was some puffiness of the upper lid, evidently an engorged vein. Congested veins stood out in the right sclera, and there was slight exophthalmos of the right eye. There was some congestion of the conjunctiva. Both eyes were sensitive to light, and dark glasses were worn. Movements of the eyes were normal except for a slight external deviation of the right eye to three degrees. The iris on the right side was congested, and there were enlarged veins on examination of the fundus. The veins on the right side of the neck were engorged and visibly pulsating. A loud systolic murmur was heard all over the right side of the neck and head, being most marked over the temporal region and the right eye. Firm pressure on the right



FIG. 4.—Case 3: Ten years after cure of pulsating exophthalmos by unilateral ligation of common and internal carotids.

common carotid stopped the bruit but caused pain. The pulse was regular, 100 per minute; blood pressure 150/90. A harsh systolic murmur was pronounced over the aortic area and was transmitted to the neck. There was no evidence of an aortic aneurysm. Roentgenograms of the skull and chest were negative. Blood Wassermann was negative. *Diagnosis:* Carotid-cavernous aneurysm of the right side.

*Operation.*—October 15, 1928: Under local anesthesia an aluminum band was applied to the common carotid of the right side, and the artery was completely occluded. The patient said the noise disappeared. The venous congestion in the eye immediately improved, but after a few weeks the noise, murmur, and eye congestion reappeared, though

they were less marked than before operation. The patient was admitted to the hospital two months later.

*Second Operation.*—January 30, 1929: Local anesthesia. Much scar tissue was found about the right common carotid at its bifurcation, resulting from the previous operation. The metal clip was found in the scar. It had cut through the artery and become encysted. Following ligation of the internal and external carotids separately with chromic catgut, the noise ceased.

The patient was examined again in February, 1939, ten years later. There had been no return of symptoms. The eyes were normal in appearance (Fig. 4) and vision was good except for changes due to age. The aortic valve systolic murmur was still present. Blood pressure 200/100. An E.K.G. was normal, and Wassermann tests were again negative. The patient had enjoyed good health and had been regularly employed as a cook for the past ten years.

*Discussion of Case 3.*—That this was a carotid-cavernous aneurysm can hardly be questioned even though no history of traumatism preceded its development. This patient had an aortic valve murmur, and though the blood Wassermann was negative, syphilitic arteriovascular disease is so common among the Negro race that we may theorize that this instance of perforation of the carotid artery into the cavernous sinus was the result of syphilitic arteritis. The patient was cured, as are 40 per cent of such cases, by unilateral obstruction of the common and internal carotid artery.

*Case 4.*—Hosp. No. 61173: A. L., white, female, age 32, entered the John Sealy Hospital in December, 1938. She had always enjoyed good health until November, 1930, when she was in an automobile accident and was unconscious for 12 hours, during which period there was bleeding from both ears and from the nose. When she regained consciousness, she noticed a swishing noise in her head which persisted without remission. After four months the right eye began to protrude and pulsate.

On April 22, 1932, Dr. R. B. Alexander of Waco, Texas, ligated the right common carotid artery with two catgut ligatures, and the artery was cut between. The pulsation apparently disappeared, but by October the condition was about the same as before the operation. On October 23, 1932, the right internal and external carotids were ligated and severed. Recession of symptoms was for a short time only. At the present time the prominence of the eye and the dilatation of the veins over the forehead reappeared. For the past two years the vision of the right eye had been failing, and now the patient was unable to read with it. The vision of the left eye was good.

Pulse 95, regular and of good volume. Blood pressure 112/70. There was a marked protrusion of the right eye, the exophthalmometer reading being 27 Mm. (Fig. 5). The veins in the sclera, above the eyeball, below the eyeball, and over the forehead were all dilated and visibly pulsating. A systolic bruit could be heard over the entire head but was loudest over the right eye and the right side of the head. With compression of the left carotids, which the patient tolerated, the bruit decreased. The eyes showed weakness of the lateral muscles. Pupils reacted to light and convergence. The right fundus had a normal disk, but the veins were tortuous. The same condition was present in the left fundus to a less marked degree. Cranial nerves were normal.

Since the carotids on the right side had already been occluded in the neck, intracranial occlusion of the right internal carotid was decided upon.

*Operation.*—January 20, 1939: An osteoplastic flap was turned down over the right frontal region (hypophyseal approach). A large amount of subdural fluid escaped when the dura was incised, and a quantity of subarachnoid fluid also escaped when the very tough arachnoid was incised. This escaping fluid, which seemed excessive in amount, left an abundance of room. Upon elevating the frontal lobe, the internal carotid artery

became quite accessible. It was smaller than the optic nerve alongside it and was purplish in color and not visibly pulsating. A large-sized silver clip was placed astride it and forced together with apparently little pressure within the vessel.

The patient showed no undue disturbance from the operation. The right eye seemed less prominent, and the dilatation of the veins was less marked. The bruit could not be heard anywhere over the head. The right pupil was dilated. Within two weeks the pulsation became faintly perceptible in the right eye. The veins grew more prominent, and the bruit could be heard over the same areas as previously, though not as distinctly. The patient could hear the noise faintly in her right ear.

Following the intracranial ligation, theoretically the blood passing through the fistula must have been backflow through the ophthalmic artery from anastomosis with branches



FIG. 5.—Case 4: Pulsating exophthalmos right eye six years after right carotids were occluded.



FIG. 6.—Case 4: Prominent ophthalmic veins present after intracranial occlusion of internal carotid and occlusion of opposite external carotid.

of the external carotid vessel on the left side. It was decided to ligate the left external carotid, and this was done under local anesthesia, February 3, 1939. The bruit was lost as soon as the artery was occluded. The pulsation of the eye ceased, and the dilated veins receded (Fig. 6).

Three days later the murmur could be heard with the stethoscope over the left eye, the left side of the head, and down the left side of the neck, although the patient could no longer hear a bruit. No sound was heard over the right eye or the right side of the head.

By March 1, 1939, the murmur was still absent over the right eye but was pronounced on the left side. The orbital veins were filled with blood under a fair degree of pressure. It was decided to inject the ophthalmic veins, and 4 cc. of 50 per cent glucose were injected. At the same time an effort was made by pressure to prevent the blood from escaping over the forehead and across the nose. When the needle was introduced into the vein, bright red arterial blood was aspirated. The patient experienced no discomfort, and there was no sign of any sclerosing or clotting following the glucose injection.

Ten days later, an injection of 1 cc. of sodium morrhuate was made in the same way. The patient experienced severe pain for 15 minutes or more. Within 24 hours there was a marked reaction, the eye being engorged with blood with a small subcleral hemorrhage and much swelling. The inflammation spread over the forehead, and the eye



condition appeared alarming, but after four or five days the reaction subsided (Fig. 7), and thrombosis was evident in the peripheral branches of the ophthalmic veins about the eye and over the forehead. Two months later the eye had receded markedly, vision had improved, and the orbital veins were not visible (Fig. 8). The murmur was still faintly audible over the eye, face and neck of the sound side but not on the affected side. The patient was quite happy about the result.

*Discussion of Case 4.*—This case is of interest in that it represents practically all standard procedures generally used for treated carotid-cavernous aneurysms, including the ligation of the carotid artery within the skull as well as the injection of the ophthalmic vein with a sclerosing solution. The



FIG. 7.—Case 4: A few days after injection of ophthalmic veins with sodium morrhuate. Marked inflammatory reaction.

FIG. 8.—Case 4: Three months after injection. Thrombosis effectual.

obstruction of the common, internal, and external carotid arteries on the affected side failed to influence the symptoms except for a short time. The ligation of the internal carotid within the skull resulted in a marked remission of symptoms. The bruit and pulsation of the ophthalmic vein and the eye ceased for several days but returned in a lesser degree. There was some recession of the eye.

Occlusion of the carotid within the skull, for pulsating exophthalmos, was first performed by Zeller, in 1911, according to Dandy, but due to an accident the patient died of hemorrhage. Hamby and Gardner (1933) ligated the artery intracranially with a silk ligature, as did Zeller. Improvement, but not complete cure, resulted immediately in this case. Dandy, in April, 1934, used a silver clip to occlude the artery intracranially and operated upon a second case in July of the same year. In both instances marked improvement resulted, and in one case there was a cure without further

treatment. In the other case, obstruction of the branches of the corresponding external carotid and later a dissection of the ophthalmic veins of the same side were necessary before a complete cure was effected.

When one examines the anatomy of the internal carotid artery, it seems quite logical to ligate it inside the skull following ligation in the neck. It may readily be seen that the only circulation left then to feed the fistula is through the ophthalmic artery with a reversal of the direction of the flow of blood. It is true that there are other very small vessels leaving the internal carotid in this segment, the carotid-tympanic, hypophyseal, and meningeal branches, but they are very small. Still one cannot ignore the compensating enlargement possible in even small arteries when circulatory demands are put upon them. Theoretically, it is quite surprising that the sinus should persist as it did in our case and one of Dandy's. Though complete cure may not result, great improvement must follow the intracranial ligation if the extracranial ligation precedes it.

We wish to confirm the statement of Dandy to the effect that the approach to the carotid intracranially and the application of a clip are comparatively easy procedures and should be accomplished with little danger of a serious accident occurring.

Because the sinus persisted after the intracranial ligation, it was evident that the ophthalmic artery was receiving blood from its peripheral anastomosis and likely from the internal maxillary and facial branches from the opposite external carotid (Fig. 9).

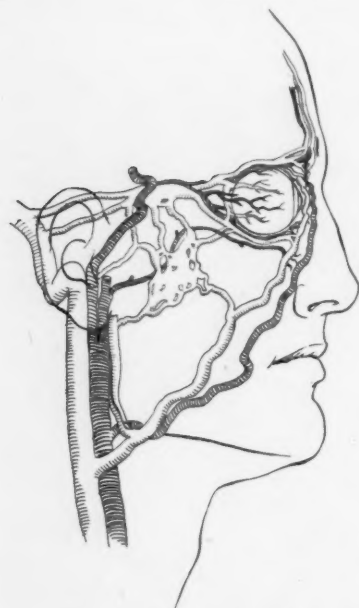


FIG. 9.—Rich anastomosis between the ophthalmic and the internal maxillary and facial branches from both sides (after Jameson).

This influenced us to ligate the left external carotid. (Our experience in ligation of the external carotid for nosebleed and tonsil hemorrhage has shown on several occasions that occlusion of one vessel alone has little influence on the bleeding, but ligation of the second vessel is quite effective, and sufficient blood is still available for the tissues supplied by the vessels.) The ligation of the opposite external carotid and its branches resulted in the complete disappearance of the pulsation from the right eye; the prominent veins decreased, and further recession of the eye resulted. The noise to the patient completely disappeared. By the stethoscope, the bruit disappeared from the right side of the head and eye but appeared distinctly over the opposite eye and the left side of the head and neck. This shifting of the murmur as in Case 1 was quite puzzling. The communicating veins between the two cavernous sinuses are quite small normally, but due to the long increased pressure within the sinuses they would have become greatly enlarged. Cases are reported by Sattler and

# INTRACRANIAL ARTERIOVENOUS ANEURYSMS

Dandy where the opposite eye became involved following occlusion of the ophthalmic vein on the affected side, which must have been due to the passage of blood through the communicating veins to the other sinus. In this instance, there was not an occlusion of the ophthalmic vein on the affected

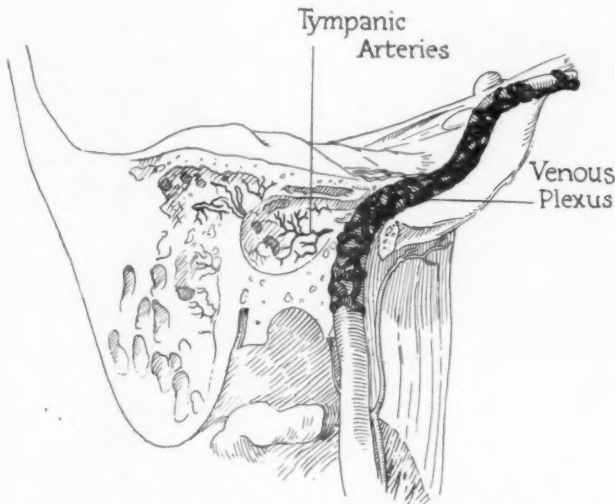


FIG. 10.—Small branches other than the ophthalmic come off the internal carotid (after Spalteholz).



FIG. 11.—Ophthalmic artery originating entirely from the middle meningeal (after Adachi).



FIG. 12.—Abnormal anastomosis between middle meningeal and ophthalmic arteries (after Adachi).

side following the ligation of the opposite external carotid. On the other hand, the obstruction of the remaining external carotid greatly lessened the blood flow and pressure in the veins of that side of the face and encouraged the blood to pass through the communicating veins to the other cavernous sinus and into the other ophthalmic vein.

This is a weak explanation of the shifting of the murmur to the unaffected side. Dr. C. T. Stone, a cardiologist of the University of Texas, suggests that this was a new murmur caused by eddies in the current of blood through the remaining internal carotid. Dr. George Herrmann, also a cardiologist, considers that "the transfer of the murmur to the left side is a part of the compensatory mechanism, which consists in dilatation of the proximal or common carotid artery, even extending as far back as the aorta, and the murmur may be due to the dilatation." These explanations of the shifting of the murmur to the opposite side of the head in Cases 1 and 4 are still not satisfactory. It is true that bilateral fistulae do occur, as reported by deSchwentz, but since there was no evidence of symptoms in the opposite eye previously, we doubt that the murmur was due to another fistula here.

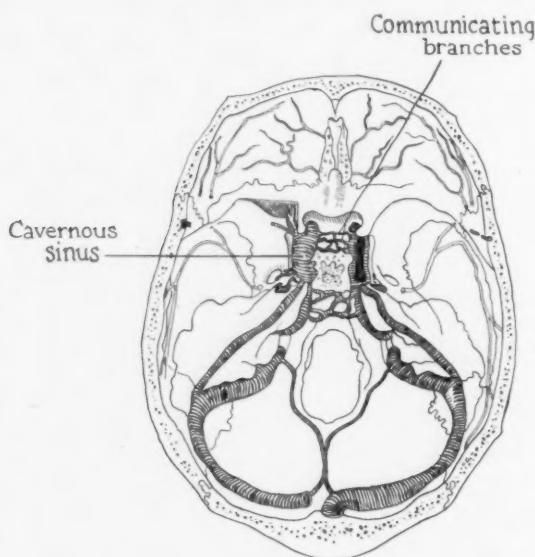


FIG. 13.—Communicating branches between cavernous sinuses (after Jameson).

*Prognosis in Carotid-Cavernous Aneurysms.*—The untreated cases may result in: (1) Death from hemorrhage in the traumatic cases at the time of injury or later. Nine deaths from hemorrhage from the nose were reported by Sattler, or 3 per cent of all aneurysms collected. (2) Damage to vision and loss of the eye is a common complication; not more than 20 per cent retain good vision, according to deSchweinitz. Nolan reports complete loss of sight in one eye in one untreated case, and in another, not only the sight in one eye was lost but almost complete blindness resulted in the other. If not complete loss of vision, there is often loss of accommodation with deviation of the eye, resulting in double vision in a great majority of cases. (3) The distress from the noise is often unbearable. Our third patient described it as "like a train puffing and roaring all the time" in her head. The distress seems augmented in the stillness of the night, making sleep difficult.

*Cures.*—A cure of the fistulae tends to follow a decrease in the arterial pressure and a slowing of the blood flow within that part of the carotid. It is generally conceded that thrombosis is the cause of the occlusion. This opinion is expressed by many writers, and that cures have resulted from thrombosis of the ophthalmic vein alone supports this theory. Still, in Dorrance's explanation of the results of serial arterial ligation, he says that "cutting down the size of the artery by decreasing the volume of blood it carries should decrease the size of the fistula, with progressive lessening of the columns transported by the proximal artery. Obliteration of its lumen could considerably reduce the size of the fistula sufficiently so as to approximate its edges and permit union."

*Spontaneous Cures* occur in from 6 to 10 per cent of cases. These may occur soon after the fistula has developed or after many years. The cure results from a thrombus occluding the communicating opening except for the possible occasional occlusion of the opening by scar contracture. Thrombosis is encouraged by slowing of the arterial flow of blood and probably thrombosis occurring from the venous side. A number of recorded cases have resulted in cures following a cellulitis about the affected eye with a thrombophlebitis of the orbital veins. Evidently the thrombosis extended into the cavernous sinus.

*Treatment.*—Treatment has been directed to such procedures as would be expected to promote thrombotic occlusion of the fistula. One of the simpler ones is prolonged compression of the carotid vessels, as well as the venous channels about the eye. Some 16 of 80 cases collected by Keller, deSchweinitz and Sattler were cured by prolonged *compression of the carotids*, and Matas, Locke, and Naffziger have devised mechanical apparatus for prolonged pressure on the carotids. The results from *obstruction of the orbital veins* have not been so favorable. *Subcutaneous injection of gelatin* has resulted in cures in a few cases, but the fear of damage to normal structures has caused it to be used only occasionally.

The *injection of sclerosing drugs* into the ophthalmic veins seems to have been little employed, though, theoretically, this should be expected to be an efficient remedy. The fear of thrombosis extending into the larger venous sinus within the skull has deterred those who have proposed such a remedy. A few injections are reported, but these occurred long ago and were with substances of uncertain sclerosing power. The extensive practice of thrombosing varicose veins at the present time with various drugs with success, probably gives us sufficient experience to use them in this way with success and less danger. The current of blood in the veins is flowing away from the fistula; therefore, the injection is against the current, and the solution will not pass easily along the ophthalmic in the direction of the sinus. We found the attempts at injecting sclerosing solutions anxious procedures, though the outcome was quite satisfactory, and we should not hesitate to inject sodium morrhuate into the ophthalmic vein again if the occasion arose. It should be more effective and a safer procedure than dissection of the veins.



*Operative Treatment.*—The following procedures have been carried out for treatment of pulsating exophthalmos:

- (1) Obstruction of the carotids extracranially with ligatures, metal bands, and fascia, partially or completely. This may take the form of:
  - (a) Ligation of the common carotid alone or preceding ligation of the internal carotid or external carotid on the same side;
  - (b) Primary ligation of the internal carotids;
  - (c) Ligation of both carotids, usually at intervals;
  - (d) Intracranial occlusion of the internal carotid after extracranial ligation.
- (2) Plugging the fistula itself with muscle by inserting it in the internal carotid in the neck (Brooks, Homby and Gardner).
- (3) Excision of the ophthalmic veins through the orbit.
- (4) Evacuation of orbital contents and attacking the fistula at the apex of the orbit.

Beginning with Travers' ligation of the common carotid upon his patient, in 1809, arterial occlusion has been by far the method most often selected for the treatment of this condition. Improvement invariably follows one or more of these procedures, but often it is only temporary. Cures have resulted in some 60 per cent of cases by carotid ligations in the neck (Locke). Intracranial ligation will increase the number of cures.

The *dangers to the brain from the ligation of the larger arteries* are well recognized. Weyth, in 1888, reports a mortality of 40 per cent following carotid ligation. Matas reports 80 cases of ligation of the common or internal carotids with 11 per cent showing cerebral complications and 7.5 per cent mortality.

Dandy says that "after the age of 35 one should regard total ligation of either common or internal carotid artery as a potential cause of death or cerebral disability, and therefore to be undertaken only after testing the collateral circulation beforehand or otherwise when the occasion leaves no escape. After age 60 or even 50, few total ligations are possible without disastrous consequences."

The age of the patient is generally considered an important factor. Still, Reid says: "We believe that the older patients are, the less likelihood there is of cerebral disturbance following ligation of the carotid artery—certainly our experience has been that it is safer to ligate the carotid vessels in older people than in young people."

These dangers may be lessened by gradual or intermittent occlusion of the vessels over several weeks' time. The ligation of the common carotid, followed after a few weeks' interval by ligating the corresponding internal, is less hazardous than primary ligation of the internal. Bilateral ligation of both common carotids has been too often fatal to be advised.

Intracranial ligations are quite feasible and should not be condemned. They have been disappointing, in that cures have not always followed, though

great improvement does result. If one could be sure that the muscle plug inserted in the carotid in the neck would not reach the circle of Willis, it would be a most direct and logical remedy.

#### CONCLUSIONS

With our present knowledge and experience, we would suggest the following line of treatment for carotid-cavernous fistula:

(1) The common carotid in the neck should be compressed for a period of time. This procedure may cure the spontaneous type or make ligation of the common carotid safer.

(2) The common carotid should next be ligated.

(3) If this is unsuccessful, after waiting a few weeks, the internal carotid should be occluded. At the same time separate branches of the external carotid on the same side should be ligated.

(4) Should symptoms persist, one has the choice of intracranial occlusion of the internal carotid, or

(5) Injection of the ophthalmic veins with sclerosing solutions such as sodium morrhuate. This should be a useful procedure and we would be inclined to give it preference. However, further experience will be necessary before its true value is determined.

(6) Ligation of the opposite external carotid will markedly influence the circulation through the fistula, and since it is without danger, it should be included as a late remedy in reducing the collateral circulation to the ophthalmic artery.

I wish to acknowledge with thanks my indebtedness to my associate, Dr. S. R. Snodgrass, for his skillful exposure of the carotid artery within the skull to which the silver clip was applied.

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DISCUSSION.—DR. MONT R. REID (Cincinnati, Ohio): As complementary to Doctor Singleton's paper it might be interesting to cite a case which is very similar to the second case he reported. The patient, female, age 11, was first operated upon by Doctor Halsted in 1911. She presented an extensive cirroid condition about the right ear, mastoid and face, associated with a "noise" in the head and a slight exophthalmos. At this operation, a very large external carotid artery was found. This was ligated and many large veins were excised. Some large arteriovenous fistulae were definitely identified. This operation was followed by a period of marked improvement, but after the lapse of seven years the condition was essentially the same as before this first operation. At the second operation I found the ascending pharyngeal, which was noted to be very small at the first operation, to be as large as a normal external carotid artery. It was ligated and other large veins were excised. For a period of four years, the condition was markedly improved, but after the lapse of eight years, I was informed that the external appearance was essentially the same as before the last operation, although the bruits and thrills were less marked and the patient was not annoyed by noises in the head.

Doctor Singleton's third case illustrates the usual futility of ligating the common carotid artery for a traumatic cavernous sinus-carotid arteriovenous aneurysm. When this is done, there is an immediate reversal of blood flow in the external carotid artery, and a large amount of blood flows backward to the bifurcation and thence upward through the internal carotid artery to keep the fistula alive and active. To avoid this, I have for many years advocated ligating the external carotid artery and occluding the common carotid with an aluminum band. This gives the maximum reduction of blood flow through the fistula and also the precaution of being able to remove easily the aluminum band and restore circulation should cerebral symptoms develop. His fourth case illustrates beautifully the additional advantage of ligating and sclerosing the supra-orbital veins in addition to the work upon the arteries of the neck.

In support of this argument, I am permitted by Dr. Frank Mayfield, of Cincinnati, to refer to one of his cases. It was a typical instance of traumatic pulsating exophthalmos. A ligation of the common carotid artery was followed by a very transitory improvement and then a rapid return of all symp-

toms and signs. A subsequent ligation of the external carotid artery was followed by so much improvement that the patient was not conscious of any bruit, although it could be heard through the stethoscope. Later, a division and thrombosis of the supra-orbital vein was followed by a complete cure. All of these operations could have been performed at one time although, as done in stages, the risk of central disturbances may have been lessened. However, when the maximum reduction of blood flow through such a fistula is sudden, the incidence of cures is certain to be higher.

I am glad that Doctor Singleton has called attention to the fact that spontaneous cures of traumatic pulsating exophthalmos do occur. He estimates the incidence from 6 to 10 per cent. Could not this incidence be increased by putting our patients to bed in the Fowler's position and instituting other measures to reduce the amount of blood flow through the fistula?

Doctor Singleton's report of a case in which he ligated the opposite external carotid artery after doing all he could on the side of the fistula is most interesting. This opens up another therapeutic procedure which may, if necessary, be brought into action in the treatment of this difficult problem of intra- and extracranial cirroid aneurysms. In the first case I cited, it seems obvious that this procedure should have been done, inasmuch as four years after the last operation temporary occlusion of the left common carotid artery affected the bruit as much as did occlusion of the right vessel.

DR. GILBERT HORRAX (Boston): My experience has been almost entirely with the cirroid type of lesion in the brain. In two or three instances we have turned down a bone flap and exposed such a cirroid aneurysm. These lesions, of course, extend below the surface, and spread out over the cortex throughout a wide area.

The patients upon whom we have performed this operation have suffered from epilepsy of one type or another, or possibly from other intracranial symptoms, and what we have done at the time of operation is to seal off by electrocoagulation a large number of the great venous trunks. They will shrivel up with the coagulating current very well, and you can effect a very extensive coagulation in that way. Whether or not that is going to prove efficacious in stopping the spread or the increase in size of these blood vessels, I am not sure, but so far the attacks have been diminished.

DR. GEORGE J. HEUER (New York, N. Y.): In the hope of provoking further discussion of the treatment of the intracranial cirroid aneurysms involving the cerebral cortex, I should like briefly to refer to six cases of this condition seen during the past few years. The patients presented themselves because of headaches, convulsions, transient hemiparesis or noises in the head. Two were young children, two young people of 14 and 20, two adults of 40 and 43. In none was there a history of injury to account for the condition. All, on auscultation, presented loud bruits either over one side or over the entire head. Ventriculograms in five of the six cases showed slight displacement or distortion of the ventricle on the side of the lesion, but of course failed to give any information regarding the extent of the lesion. An attempt to delineate the extent of the lesion by the use of thorotrast was made in three cases. In one, it was successful, and no harm followed its employment.

Our treatment of these patients as yet may be spoken of as tentative or palliative and it is for this reason we should be grateful for suggestions. In two of the cases, we have performed ligation either of the right or left external and common carotid arteries. The result in one has been steady improvement, in the other, slight if any improvement. In two cases, a cranial exploration and decompression was combined with the administration of from 3,600

R. units to 9,600 R. units of roentgenotherapy. In one case, the headaches have improved and the frequent convulsive seizures reduced to one during the past three years; in the other cases, there has not been any improvement. In one case, a cranial exploration and decompression was followed by ligation of the right external and common carotid arteries and the administration of 13,000 R. units of roentgenotherapy. The result has been a diminution in the number of convulsive seizures. One case thus far has refused treatment. These cases will be reported in more detail at a later date.

DR. WILLIAM JASON MIXTER (Boston): It seems to me that Doctor Singleton has given us a very concise account of the handling of two quite distinct groups of cases, because the arteriovenous aneurysms of the cavernous sinus must be considered quite separately from the cirroid aneurysms of the cranium or the brain.

I should think that his plan of action in regard to the cavernous aneurysms was excellent. I do not know whether I would agree with him absolutely in his choice of the last two methods, because I am rather afraid of sclerosing solutions in a place like the ophthalmic veins; nevertheless, his result in this case has been so good that I think he has the right to prefer it.

As regards the other group of cases which he mentioned, the two cirroid aneurysms, there we are dealing with a different problem, and we have to evaluate each particular case very much on its own merits according to the structures involved.

In one of his cases, the first, there was evidently considerable involvement of the cerebrum, and I wonder whether the boy's paralysis was due entirely to the ligation of the carotid or whether it was simply from progress of the lesion in the cerebrum.

These cases require a tremendous amount of care in recognizing the vessels involved, and I think the only thing that I would suggest would be the use of thorotrast, which in such cases as this is of great value in demonstrating where the larger trunks lie.

DR. FRANCIS GRANT (Philadelphia): With regard to Doctor Singleton's problem of exophthalmos on the side of the aneurysm, we have recently had a case in which the boy had been relieved by external ligation of various carotid vessels, and consequent upon that the exophthalmos had continued with the venous engorgement. We explored that case for the possibility of either clipping the carotid intracranially or getting rid of the vein, and we took off the roof of the orbit. I have had occasion to do that once or twice for orbital tumors. It is a very simple thing to do. In this particular case the vein was engorged in the orbit and it was a relatively simple matter to ligate them in that area. Furthermore, I think with the removal of the roof of the orbit the exophthalmos tends to decrease because you obtain decompression upward into the cranium. The exposure that you employ would be precisely that for ligation of the carotid intracranially, and, as I say, the removal of the orbital roof is not particularly difficult. So if you happen to be faced with one of these problems of enlarged veins, that would seem to be a possibility for its control.

DR. ALBERT O. SINGLETON (closing): I am very glad to have these able discussions recorded with this paper.

The real object of treatment is to occlude the sinus. In the carotid-cavernous cases, which are the ones that have created so much interest, it is a thrombosis that stops the fistula. If one can slow the blood stream enough to allow clotting to occur, there is a cure. This usually is attempted by an



attack upon the arteries, but, as Doctor Reid pointed out, a complete stopping of the circulation through the carotid, that portion where the fistula is located, is apt to result in cerebral symptoms of a severe nature.

The observations are that many of these patients have been cured by thrombosis of the ophthalmic vein, as in cellulitis, or thrombophlebitis, and apparently the thrombosis does not extend back farther than the cavernous sinus, or far enough into the venous sinuses to be of great danger to the venous circulation in the brain.

So I am strongly of the opinion that the injection of sclerosing solutions into the ophthalmic veins will prove to be a very useful remedy in the treatment of this condition. The current of blood is running away from the brain and will not carry the solution into the cavernous sinus. If thrombosis can be started in the ophthalmic veins, it may, as in this case, extend back to the sinus and occlude the fistula without endangering the circulation.

## MYASTHENIA GRAVIS AND TUMORS OF THE THYMIC REGION\*

REPORT OF A CASE IN WHICH THE TUMOR WAS REMOVED

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THIS PAPER deals in the main with myasthenia gravis and certain abnormalities of the thymus, and the possible relationships of these conditions to each other. It is recognized that any consideration of these subjects must be limited in scope because of the incompleteness of our knowledge. With regard to tumors of the thymus Ewing<sup>1</sup> states: "No group of tumors has more successfully resisted attempts at interpretation and classification than those of the thymus. The problems involved include those which have complicated the embryologic and histologic study of the gland, while added difficulties arise from the comparative rarity and considerable diversity of the tumors, and from the somewhat imperfect knowledge of the general pathology of the thymus." Thus, we wish to emphasize, at the beginning, that knowledge concerning myasthenia gravis and thymic tumors, and the relationship of these to each other, is relatively meager.

*Myasthenia Gravis.*—Myasthenia gravis is a disease characterized by abnormal fatigability of muscles, usually, but not always, attended by characteristic lymphocytic infiltration of these and other organs,<sup>2</sup> and frequently by abnormalities of the thymus, such as failure of involution and neoplasms.<sup>3, 4</sup> There are no characteristic or constant lesions of the central nervous system. The occurrence of spontaneous remissions indicates that whatever the underlying disorder may be, the changes it produces are not irreversible in nature.

Norris<sup>5</sup> recently stated: "Historically, myasthenia gravis has been regarded from widely differing points of view. At first it was believed to be a disease of the central nervous system, then regarded as an entity whose picture was produced by metastases from a malignant thymus, and then as a primary disease of the striated musculature of the body. Our point of view then seemed to be changing toward classifying it among the diseases of general metabolism, and finally the malady seems to be best regarded as a disturbance of the neuromuscular mechanism, possibly upon an endocrine basis." The prevailing theory at the present time is that there is in myasthenia gravis some interference with the transmission of impulses across the myoneural junction. However this may be, the precise etiology of the disease is unknown. The mechanism underlying its most outspoken manifestations, weakness and abnormally rapid fatigability of muscles, is poorly

\* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

understood. Yet, in spite of this lack of knowledge, certain drugs have been employed in its treatment with a moderate degree of success. Among these are ephedrine, glycine, prostigmin and guanidine.<sup>6</sup> The response to prostigmin, in terms of temporarily improved muscle strength and endurance, has been found to be so constant that a therapeutic test with this drug is considered the best diagnostic sign of myasthenia gravis.<sup>7</sup>

*Tumors of the Thymus.*—An excellent description of the variations in structure which may be encountered in thymic tumors is given by Ewing.<sup>1</sup> He stated: "A full survey of the structural variations reveals, at one extreme, a mixed process involving lymphocytes and reticulum cells, with giant, plasma, and eosinophile cells, producing a structure nearly identical with Hodgkin's granuloma. At the other extreme, are nearly pure tumors of rounded or polyhedral reticulum cells, *i.e.*, lymphosarcoma and carcinoma. . . . Hence the conclusion is reached that the great majority of the thymus tumors, and especially the mixed growths, represent infectious granulomata, or particular forms of cell overgrowth arising on the basis of an infectious granuloma." Since tumors of the thymic region are relatively uncommon, and as one observer usually has the opportunity to study only a few lesions and because there is this difficulty in interpretation of the structure, it is not surprising that various points of view concerning the nature of the tumors have been expressed. Regarding nomenclature, Decker<sup>8</sup> stated: "Thus by thymoma, Brown means carcinoma; Crotti all tumors; Bell nonmalignant tumors; Margolis all tumors of parenchymal origin." It is generally agreed that benign tumors of the thymus are encountered less frequently than malignant ones. Crosby<sup>9</sup> published, in 1932, a review of all malignant tumors of the thymus reported up until that time. The total number was 166, 122 of which he classified as sarcomata and 44 as carcinomata. The review of malignant tumors of the thymus was brought up to date by Decker,<sup>8</sup> in 1935, at which time the total number was 208. Several have been recorded since that time. Reports of benign tumors of the thymus are few in number and in most instances they have occurred in patients with myasthenia gravis.

*Abnormalities of the Thymus and Myasthenia Gravis.*—That there may be more than a casual relationship between myasthenia gravis and abnormalities of the thymus is suggested by their frequent association. The first description of a thymic tumor in association with myasthenia gravis was reported by Weigert,<sup>3</sup> in 1901. Bell<sup>4</sup> collected, from the literature of 1901-1917, 56 cases of myasthenia gravis in which autopsies or operations had been performed. Twenty-seven of these exhibited abnormalities of the thymus. A diagnosis of thymoma was made in ten and the remainder were recorded as having either a persistent or an enlarged thymus. The tabulation was continued by Norris<sup>5</sup> and brought up to 1936. Among a total of 80 necropsy reports on patients with myasthenia gravis, including those of Bell, 35 record lesions of the thymus. He stated: "I am of the opinion that pathologic changes may be found in the thymus in cases of myasthenia gravis in direct ratio to the care with which they are sought." A careful search

TABLE I  
 LESIONS OF THE THYMUS IN MYASTHENIA GRAVIS  
 (Collected by Bell<sup>4</sup> and Norris<sup>5</sup>)

Case No.	Year	Author	Patient		Thymus	
			Age	Sex	Enlarged or Persistent	Tumor
1	1901	Laquer and Weigert	30	M.		5x5x3 cm.
2	1901	Weigert	—	—		A tumor
3	1901	Burr and MacCarthy	21	F.	Enlarged	
4	1902	Hödlmoser	18	F.	Enlarged	
5	1902	Link	43	M.	3 cm. long	
6	1904	Hun, Blumer and Streeter	32	M.		5x5x5 cm.
7	1905	Burr	30	M.	22 Gm.	
8	1905	Buzzard	40	M.	9.5 Gm.	
9	1905	Buzzard	40	M.	59.4 Gm.	
10	1905	Buzzard	28	F.	41 Gm.	
11	1905	Dupré and Pagniez	32	F.	8 Gm.; persistent	
12	1907	Steinert	Elderly	F.	Persistent	
13	1908	Meyer	47	M.	Enlarged	
14	1908	Booth	11	M.	11x5.5x1 cm.	
15	1908	Marinesco	31	F.	Persistent	
16	1908	Mandlebaum and Celler	52	M.		5x3.5x2 cm.; 20 Gm.
17	1908	Wiener	67	F.		A tumor
18	1908	Meggendorfer	47	M.		A tumor
19	1909	Boudon	17	F.	36 Gm.	
20	1911	Moorhead	25	F.	Persistent	
21	1911	Symes	21	F.	11.4 x7.6cm.	
22	1911	Oppenheim	40	F.		A tumor
23	1912	Klose	23	M.		A tumor
24	1913	Schumacher and Roth	19	F.	49 Gm.	
25	1914	Claude, Géry and Porak	51	M.		A tumor
26	1915	Hart	—	—		5x4x4 cm.
27	1915	Hart	30	F.	Persistent	
28	1917	Bell	58	M.		6x3.6x3.5 cm.; 60 Gm.
29	1921	Bouttier and Bertrand	Mid. age	F.	Persistent	
30	1923	Mella	48	M.		7.5x5.5x2.5 cm.
31	1929	Alter and Osnato	31	F.		9x7x6 cm.
32	1934	Brem and Wechsler	27	F.		4x2.5 cm.
33	1934	Brem and Wechsler	54	M.		9x3 cm.

# TUMORS OF THYMUS

TABLE I (Continued)

Case No.	Year	Author	Patient		Thymus	
			Age	Sex	Enlarged or Persistent	Tumor
34	1936	Norris	37	F.		10x4x4 cm.; 57 Gm.
35	1936	Norris	33	M.		5.8x4.8x1.2 cm.; 16.6 Gm.
(Collected by Authors)						
36	1918	Froboese-Thiele and Lesche- ziner	27	F.	Persistent. 15 Gm.	
37	1919	Pulay	17	F.	Enlarged	
38	1923	Mott and Barrada	—	M.	70 Gm. Thick fibrous cap- sule.	
39	1930	Auerbach	53	F.		Pigeon-egg in size
40	1931	Halpern and Popper	43	F.		9x5x5. Encapsu- lated
41	1932	Lowenthal	63	F.	Enlarged. 26 Gm. 8x4.5x 1.5 cm.	
42	1932	Symmers (Case 14)	52	M.		12.5x7.5x2.5 cm. Smooth
43	1933	Zajewloschin	30	F.		5x4x1.4 cm.
44	1935	Gold	31	F.		4 cm. in diameter, Round tumor
45	1936	Butt	—	—		Tumor
46	1936	Butt	—	—		Tumor
47	1936	Alajouanine, Hornet, Thurel and Andre	40	M.		Large Tumor
48	1937	Alajouanine, Hornet and Morax	48	M.		Ovoid tumor. Size small hen's egg
49	1937	Norris	52	M.		63 Gm. 9x6x3.5 cm. Numerous cysts
50	1937	Adler	40	F.		Size of child's head. Opera- tion. Death
51	1937	Obiditsch	50	M.		7x4x3 cm.
52	1937	Obiditsch	47	M.		Size of man's fist. Operation. Death
53	1938	Peer and Farniacci	20	M.		136 Gm. 12x6.5x 3.5 cm.
54	1939	Authors' case	24	F.		Cystic tumor, 6x5x3 cm.



of the literature has resulted in the collection of 18 additional cases<sup>10</sup> to 26 of myasthenia gravis with abnormalities of the thymus, determined by autopsy or operation. Most of these have been reported since 1935. Thus, there have been reported 53 instances of abnormalities of the thymus in approximately 110 autopsies or operations upon patients with myasthenia gravis. Thirty-one of these are classified as tumors and 22 are recorded as exhibiting enlargement or persistence of the thymus (Table I). It is doubtful if the incidence of the association of myasthenia and abnormalities of the thymus is as high as these figures indicate, since the autopsy findings in patients with myasthenia are more apt to be reported if there is present some abnormality such as a tumor of the thymic region. On the other hand, it is possible that small tumors may be overlooked at necropsy unless a careful search is made.

In addition to the reports which are listed in Table I, and which are described in the literature in moderate detail, there are a number of casual references to the association of myasthenia gravis and thymic abnormalities. Gordon Holmes<sup>26</sup> states that there were either tumors or enlargements of the thymus in six of the eight cases of myasthenia gravis which he had examined at autopsy. Greenfield<sup>26</sup> stated that the thymus was persistent in three subjects he examined postmortem. In addition, there are a number of reports on roentgenologic evidence of anterior mediastinal tumors in patients with myasthenia gravis.

The collected series of Norris<sup>5</sup> (1936) and Lievre<sup>27</sup> (1936) do not agree in all respects. Lievre assembled observations on 67 patients with myasthenia in whom complete autopsies were performed. A tumor in the thymic region was found in 24 of these and persistence or hypertrophy of the thymus in 32. No anomaly was noted in the remaining 11 patients. The mean weight of the tumors was 60 Gm. and the mean diameter was 5 cm. Their usual location was in the anterior mediastinum, immediately behind the sternum and in contact with the superior part of the pericardium. Lievre, as well as others, has observed that most of the thymic tumors reported in individuals without myasthenia were malignant, whereas a large percentage of the benign ones occurred in myasthenics. One of the exceptions is an "essentially non-malignant" tumor of the thymus weighing 2,235 Gm., reported recently by Andrus and Foot.<sup>28</sup> A diagnosis of myasthenia was not made in this patient, a boy, age 13, although abnormal fatigability was a prominent symptom.

Bell<sup>4</sup> stated that the thymic tumors occurring in myasthenia gravis form a distinct group. "They are all comparatively small, benign growth, composed of young thymic tissue. Many are hemorrhagic." Norris<sup>5</sup>,<sup>22</sup> is of the opinion that the pathologic findings which are present in the thymus in myasthenia gravis are best interpreted as conditions of greater or lesser degrees of epithelial hyperplasia. "When the hyperplasia is extreme, a localized, and at times encapsulated, tumor-like mass is formed. In these instances of more extreme hyperplasia the usual lobular structure of the thymus may be completely obliterated and only very few lymphocytes and

almost no Hassall's corpuscles may be found in the epithelial mass. On the other hand, when the hyperplasia is considerable but less extreme, the lobulation of the thymus may persist and the corpuscles of Hassall and lymphocytes may be relatively more numerous." Lievre<sup>27</sup> states that thymomata contain lymphoid and epithelial elements and rarely Hassall's corpuscles. Brem and Wechsler<sup>29</sup> found lymphocytes, plasma cells, large polyhedral cells and occasionally giant cells and Hassall's corpuscles. Obiditsch<sup>24</sup> states that there is a preponderance of small round cells in benign tumors of the thymus associated with myasthenia gravis, whereas they are almost entirely epithelial in type in the thymic tumors not associated with myasthenia.

In spite of difficulties in interpreting the classification of thymic tumors, it is our impression that there has been recorded only one case in which myasthenia was associated with a malignant thymic growth. This is the case reported by Meggendorfer,<sup>30</sup> in 1908. However, Bell<sup>4</sup> expresses some doubt concerning the correctness of the classification of this tumor. In any event, it would seem highly probable that hyperplasia or benign tumors of the thymus and myasthenia gravis accompany each other in a large percentage of cases, whereas malignant tumors of the thymus and myasthenia are rarely associated.

*Operations upon the Thymus in Patients with Myasthenia Gravis.*—The literature contains the records of only four attempts to influence the course of myasthenia gravis by surgical intervention. The first of these was reported by Schumacher and Roth,<sup>31</sup> in 1913. The patient, a female, age 21, had definite and severe hyperthyroidism and myasthenia gravis. There was a symmetrical increase in the size of the thyroid gland with a marked increase in its vascularity. Roentgenologic examination revealed a mass in the anterior mediastinum which was thought to be an enlarged thymus. The first operation consisted of ligation of the right superior thyroid artery and vein. Little if any improvement resulted. The second operation (Sauerbruch) consisted in the removal of an enlarged thymus which weighed 49 Gm. Examination of this gland showed hypertrophy without tumors. The picture was that of a fetal thymus. Hassall's corpuscles were numerous. A diminution in the signs and symptoms of myasthenia followed this operation. A subtotal thyroidectomy was performed 18 months subsequently, following a severe thyroid crisis. The patient improved but was not cured of myasthenia at the time of the report. The second case of myasthenia in which an operation upon the thymus was performed is mentioned very briefly by Haberer<sup>32</sup> in a report of operations upon the thymus for other conditions. The patient was a man, age 27. There was no evidence of enlargement of the thymus gland. A partial thymectomy was performed and the thymus was described as being in a state of involution. When examined three years subsequently, the patient appeared to be improved. The third case is reported by Adler.<sup>23</sup> In this instance, a benign thymic tumor the size of a child's head was removed by Sauerbruch. The patient died eight days subsequently of mediastinitis. The fourth case is that reported by Obiditsch,<sup>24</sup> in which the

tumor was the size of a man's fist. It was removed by Sauerbruch and the patient died five days later as a result of a Streptococci infection. Lievre,<sup>27</sup> in 1936, stated that there existed no published report of the successful removal of a thymoma. Andrus and Foot,<sup>28</sup> (1937) in reporting the removal of an "essentially nonmalignant" tumor of the thymus in a boy without myasthenia gravis, states: "No case that we can find has survived operative removal of a thymoma more than a few days, which makes our case unique."

**Case Report.**—The complete record of this patient including her preoperative course has been reported in detail by two of us (Riven and Mason<sup>33</sup>). Only the salient features will be recounted here.

J. H., white, female, age 19, was referred, in 1934, by Dr. Walter Dandy of Baltimore and Dr. C. D. Walton of Mount Pleasant, Tenn., with a diagnosis of myasthenia gravis. Typical symptoms of this disease appeared at age 16 in February, 1932, and persisted for approximately three months. The muscles of the face, jaws and eyes were involved. The next exacerbation occurred in February, 1933, and persisted for five months. There was difficulty in talking and in using the legs and arms as well as the muscles involved in the first attack. The next recurrence, in February, 1934, was even more severe and symptoms persisted for seven months. She fell a number of times when attempting to walk. She was first seen in the Vanderbilt Hospital in September, 1934, in a partial remission, and the positive findings were limited to the presence of dysfunction of the muscles of expression and some weakness of the muscles of the neck, abdomen and extremities. The basal metabolic rate was normal. Roentgenologic examination of the chest (Dr. C. C. McClure) revealed a sharply circumscribed, dense shadow just anterior to the left auricle, extending somewhat to the left and not seen to the right of the midline. Roentgenotherapy was instituted and the shadow of the mass in the anterior mediastinum decreased in size. Therapy otherwise consisted of ephedrine and glycine. Roentgenotherapy was again administered in January, 1935.

The next severe relapse occurred in December, 1935. She complained of progressive weakness, ptosis of the eyelids, diplopia, indistinct vision and difficulty in talking, chewing and swallowing. The return of these symptoms had been gradual. The facial expression was languid and the speech was slow and slurred. There was partial ptosis of the eyelids. The mouth was drawn to the right and the left side of the face was smoother than the right. The masseter muscles were weak. The grip in the right hand was weaker than that in the left and both hands tired very quickly. The muscles of the trunk and lower extremities became fatigued quite readily. Roentgenologic examinations showed that the mass in the mediastinum had returned to a slightly larger size than that observed prior to the roentgenotherapy.

On December 28, 1935, treatment with drugs was suspended for the purpose of completing certain metabolic studies. Several days later, the condition of the patient became suddenly worse. Prostigmin was administered and dramatic improvement of approximately three hours' duration was obtained. In addition, therapy with glycine and ephedrine was instituted. Increasing amounts of prostigmin became necessary and during the latter part of January, the patient received as much as 9 cc. in 24 hours. On the morning of January 31, 1936, the patient asked that the 5 A.M. dose of prostigmin be omitted. This was done. She was not observed again until 7:15 A.M., at which time she was extremely cyanotic. Respiratory movements were barely perceptible. Vomiting had occurred and she was incontinent of urine and feces. Artificial respiration and prostigmin therapy were instituted and normal breathing was resumed in approximately ten minutes.

During February, the patient received a course of four roentgen ray treatments over the region of the thymus but this did not cause any decrease in the size of the mediastinal shadow or any immediate improvement early in March. Less prostigmin was required and the dose was reduced gradually. During April, the patient was able to be out of

## TUMORS OF THYMUS

bed most of each day. She gained in weight and strength. By May, she was considered to have attained a good remission.

Dr. Barney Brooks and Dr. Edward Churchill were consulted, and it was agreed that the tumor mass in the anterior mediastinum should be removed. Because of the marked incapacity the patient had experienced, because it seemed possible that removal of the tumor might result in improvement, and because the risk inherent in the operative procedure was judged to be not great, this course was decided upon.

*Operation.*—May 26, 1936 (Doctor Blalock): An intratracheal tube was introduced and the anesthesia consisted of nitrous oxide and oxygen and a small amount of ether. An incision was made beginning in the suprasternal notch, extending down the midline of the sternum and curving slightly to the right at the third interspace. By the use of sharp and blunt dissection, an index finger was introduced through the suprasternal notch beneath the sternum into the anterior mediastinum. By a similar procedure, an index finger was introduced beneath the sternum through the third right interspace. After pushing the pleura and other structures laterally, the sternum was split in the midline with shears. It was cut across in a transverse direction at the level of the third interspace.



FIG. 1.—Photograph of tumor, measuring approximately 6x5x3 cm., removed from thymic region.

A self-retaining retractor was inserted and a good exposure of the anterior mediastinum was obtained. A reddish-purplish tumor was visible in the thymic region. It was densely adherent to the neighboring structures. By sharp and blunt dissection it was freed from the surrounding structures and the vessels at its base were ligated with silk. The tumor was regular in outline and was soft. No other abnormalities were visualized. Some of the tissues surrounding the tumor had the appearance of fat. No tissue was definitely identified as being thymus. The space left by the removal of the tumor was obliterated in part by suturing the neighboring structures together. Several holes were made in the sternum by the use of a drill and the opposite sides were approximated with catgut sutures. The third and fourth costal cartilages were approximated by an encircling suture of catgut. The anterior periosteum of the sternum was closed with interrupted silk sutures. Similar sutures were used in closing the subcutaneous tissues and skin. One cubic centimeter of prostigmin was administered before the operation was begun and a second dose was given during the course of the operation. There were no untoward incidents during the operative procedure and the patient was returned to the ward in good condition.

*Pathologic Examination.*—*Gross:* The cystic tumor was quite evidently benign. It was smooth, well encapsulated and measured approximately 6x5x3 cm. (Fig. 1). Its wall varied from 4 to 8 Mm. in thickness. It contained thin, brown fluid and shreds of brown, seminecrotic material.

Sections of the tumor were studied by Dr. E. W. Goodpasture and the following is from his report:

*Microscopically*, "the sections show a fibrous wall lining a somewhat spherical mass, the interior of which, so far as can be judged from the small portions attached to the fibrous wall, is composed of fibrin, red cells and precipitated protein. There is no evidence in these sections that there are remnants of a previously organized tissue which has undergone necrosis. The fibrous wall consists of essentially three layers. An outer thin adventitial layer in which there are fairly large blood vessels, both arteries and veins. Here and there are extravasations of red blood cells and about some of the smaller vessels there is an accumulation of lymphocytes and plasma cells. Underlying this coat there is a dense hyaline collagenous membrane arranged more or less in laminations measuring about one millimeter in thickness through which traverse a few blood vessels. Some of the arteries in this layer show an endarteritis with thickening of the intima which encroaches upon the lumen. Beneath this second coat of hyalinized fibrous tissue, there is a layer of granulation tissue of varying thickness and degrees of degeneration. In some areas of the granulating layer there are foci of degeneration in which clefts formed by cholesterol crystals remain. Some of these spaces have no reaction about them, others are lined by mononuclear phagocytes or foreign body giant cells. Frequently about such areas the granulation tissue is filled with "foam cells" representing phagocytes previously filled with lipid materials. In still other areas there is a considerable amount of orange amorphous pigment representing hemosiderin. Occasionally, small deposits of calcium are also noted. There is very little cellular exudate within the granular layer although there are numerous focal accumulations, usually perivascular, of plasma cells intermixed with lymphocytes. Blood vessels and capillaries are numerous and they extend inwardly into the fibrinous material which is being organized thereby (Figs. 2, 3 and 4).

"In no section which I have examined is there microscopic evidence of thymic tissue of any sort nor of any other previously organized tissue.

"It would appear that the encapsulated mass had been distended by extravasated blood, consisting of red blood cells, fibrin and serum, which is gradually becoming organized by granulation tissue.

"Aside from the history and location of the mass the only diagnosis that I can make from the examination of the microscopic section is: An encapsulated fibrino-serousanguineous exudate; degenerative changes in the capsule indicated by hyalinization, necrosis, cholesterol crystal deposits, foreign body reaction, hemosiderin pigmentation, slight calcification, hyalinization of connective tissue, and endarteritis at times obliterating. The etiology is not evident.

"In attempting to interpret the pathologic picture present, it seems quite likely from the position of the mass and from clinical relationships that it represents the remains of a necrotic thymic tumor. The necrosis and fibrosis might reasonably be explained on the basis of roentgen ray irradiation."

The patient had a very smooth postoperative course. Prostigmin was administered in small amounts for the first eight days following the operation and it was then discontinued. She was transferred to the medical service 12 days following operation and she was discharged from the hospital on the twenty-first day.

*Subsequent Course.*—A part of the first winter following the operation was spent in Florida where she remained for four and one-half months. Her tolerance to exercise was rather poor when she arrived there but this improved rapidly and very shortly she was able to swim and dance. She would often walk as much as ten miles a day. She would occasionally, once every month or two, take a little prostigmin by mouth. This was usually on occasions when she had exercised a great deal during the day and was going to a dance at night. She returned to Nashville, March 30, 1937. The striking difference noted at that time was that her smile appeared essentially normal. There was perhaps a slightly drawn expression around the nose which had persisted.

She contracted a severe respiratory infection shortly following her return from Florida and she noted some difficulty in masticating her food and there was a less notice-



Fig. 2.—Photomicrograph showing wall of cystic cavity. From above downward: Thin adventitial layer, dense hyaline collagenous membrane arranged in lamellae, layer of granulation tissue, fibrin, red blood cells and precipitated protein. Hematoxylin and eosin. ( $\times 35$ )

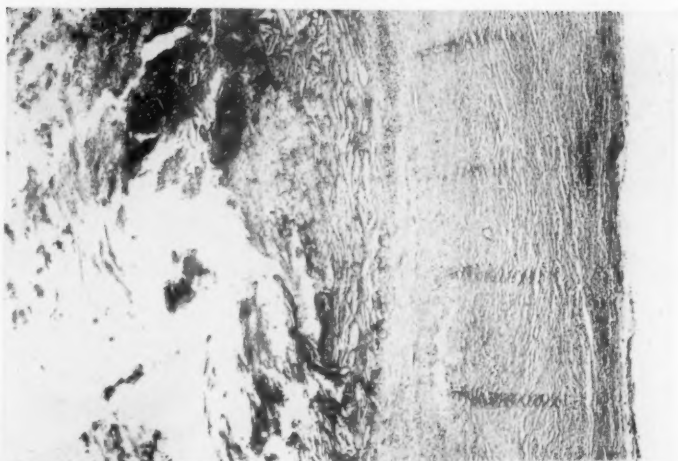


Fig. 3.—Photomicrograph showing cholesterol deposits, foam cells, and endarteritis (left lower part of field). Hematoxylin and eosin. ( $\times 44$ )



Fig. 4.—Photomicrograph showing, from above downward, lymphocytes and plasma cells about some of the smaller blood vessels, cholesterol clefts surrounded by foreign body giant cells, from cells and granulation tissue. Hematoxylin and eosin. ( $\times 120$ )



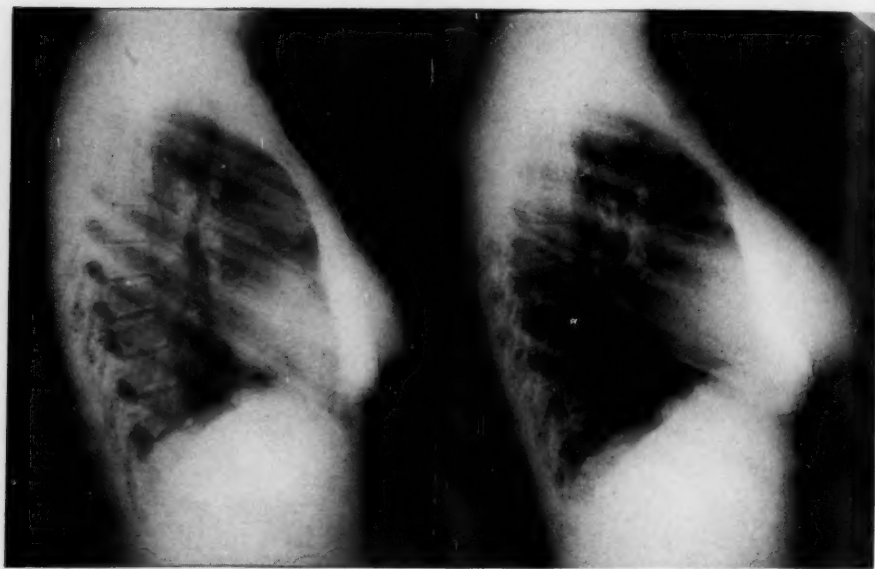


FIG. 5.—Preoperative, lateral roentgenogram of chest showing tumor in anterior mediastinum.

FIG. 6.—Lateral roentgenogram taken one year following the removal of the tumor.



FIG. 7.—Photograph of patient taken two weeks following the operation.



FIG. 8.—Photograph of patient taken one year following the operation.

able return of some of her other symptoms. She returned to the hospital for a stay of two days. The symptoms cleared up in a short while.

For the past two years, there has been no recurrence of symptoms. She has not gone to a warmer climate during the winter, spending one winter in Washington, D. C., and one in Virginia without a return of symptoms of myasthenia. On a few occasions she took a small quantity of prostigmin by mouth before undertaking severe exercise such as a game of tennis. During recent months she has not taken prostigmin on any occasions.

Roentgenograms of the chest before and after operation are shown in Figures 5 and 6. Unfortunately, a preoperative photograph of the patient cannot be located. A photograph taken two weeks following the operation and another taken a year subsequently are shown in Figures 7 and 8.

In summary, during the three years following the removal of a tumor of the thymus region, a patient who had been incapacitated for months every year for four years has had only one mild recurrence which lasted only a few days. This was associated with a severe respiratory infection.

*Discussion.*—It is generally agreed that the thymus, at least in the adult, is a nonessential organ. For this reason, we felt that the chief question to be decided in considering operation in our case was whether or not the possible gain was sufficient to justify the risk associated with the major operative procedure. Although there is no unanimity of opinion concerning the physiologic functions of the thymus, some of the views on this subject will be discussed.

Five general methods of study of thymic function have been employed, in which the effects of the following procedures upon various experimental subjects have been observed: (1) Removal or destruction of part or all of the gland at various ages; (2) excessive feeding of thymic tissue or extracts; (3) multiple injections of extracts of the organ; (4) implantation of additional thymic tissue; and (5) combinations of these methods. In addition, the effects on the thymus of induced alterations in the other ductless glands have been noted. Present knowledge with respect to the first four categories may be summarized as follows:

(1) *Effects of Removal or Destruction of the Thymus.*—An extensive literature upon this subject has developed since the original experiments of Restelli,<sup>34</sup> in 1845, from which only one conclusion may be drawn with certainty, *i.e.*, the thymus is not essential to life. The findings of Basch,<sup>35</sup> Klose and Vogt,<sup>36</sup> and Matti<sup>37</sup> that thymectomy led to abnormalities in calcium metabolism were shown in the excellent study and review of Park and McClure<sup>38</sup> to be the result of the diet and confinement in a cage rather than the direct consequences of thymic extirpation. The numerous claims that the gonads were affected by thymectomy have been dealt with in a critical review by Anderson.<sup>39</sup> From a careful study of the literature, and from extensive experimental data of her own, she felt able to state: "We may conclude that thymectomy does not prevent, hasten, or delay the arrival of sexual maturity, and it does not prevent the occurrence of normal litters. In other words, aside from the immediate effects of the operative injury, it has not been shown that deprivation of the thymus, even in early life, has any effect upon the development and function of the sexual apparatus." In

her own experiments with rats one series was thymectomized at the age of one day.

Andersen's point of view may need modification in the light of some of the more recent evidence. Thus Shay *et al.*<sup>40, 54, 55</sup> have destroyed the thymus of young rats by roentgen rays and find that there is an arrest in the development of the spermatogenic portion of the testes, leading to physiologic castration, with castrate changes in the pituitary. The changes progress until about the one hundredth day of life during which time the males are sterile. After this period, reparative processes occur, fertility returns, and the testes and pituitary are normal again at 150 days. The reparative processes set in about the time the thymus passes the peak of its development and commences involution. Females were not affected.

Einhorn and Rowntree<sup>41, 42</sup> studied the effects of thymectomy upon successive generations of rats and obtained retardation of growth, and to a lesser extent, somatic development, commencing in the second (F<sub>1</sub>) generation, and becoming more pronounced thereafter. Only a limited period of growth is affected (ten to 50 days), the rats operated upon eventually attaining the same size as controls. All thymectomies were performed at from 17 to 24 days of age and the glands of both parents had to be ablated in order to secure the observed effects.<sup>42</sup> In any given generation, the growth curves of thymectomized and nonthymectomized litter mates are the same. No definite interpretation has been advanced for this curious cumulative effect which is the reverse of that resulting from injection of thymus extract (*vide infra*).

(2) *Excessive Feeding of Thymic Tissue or Extracts.*—The literature on this phase of thymus physiology is summarized by Gudernatsch,<sup>43</sup> who made the first observations on the effect of feeding thymic tissue and obtained improved growth and retarded metamorphosis in tadpoles. In the case of rats, improved growth but no retardation of differentiation was observed. Similar results were obtained by Ratti.<sup>44</sup> The objection that these results are simply due to improved nutrition is rendered unlikely by the fact that injected purified extracts of thymus increase growth (*vide infra*).

(3) *Effects of Multiple Injections of Thymic Extracts.*—The first experiments in this category were reported by Asher,<sup>45</sup> who found that the injection of a thymic extract, "thymocrescine," had an accelerating influence on the growth rate of first generation rats. In later papers from his laboratory, the purification of this substance is reported<sup>44, 46, 47, 48, 49</sup> and as little as 1 mg. injected per day was found to be effective. The active substance contains peptides, amino-acids and sulphur—possibly as cysteine, cystine or glutathione.

The most striking results by this approach have been reported by Rowntree and his collaborators.<sup>50, 51, 56, 57</sup> Multiple injections of a dilute HCl extract of calf thymus (Hanson extract) into successive generations of rats causes a striking precocity which is first observed as early as the second generation, and is cumulative through several succeeding generations. Only the early growth period is effected, and the effect is lost upon interruption of the injections during any given generation. Only the females need be in-

jected.<sup>52</sup> "Hanson extract" also contains reduced sulphur compounds and ascorbic acid, and Rowntree's<sup>53</sup> group has recently reported that some but not all of the effects of thymus extract may be obtained by injecting cysteine and glutathione and ascorbic acid.<sup>52</sup>

In a brief report, Adler<sup>23</sup> has stated that thymus extract (preparation not described) injected into dogs produces a syndrome resembling myasthenia gravis. He further states that the weakness and collapse exhibited by these animals is immediately abolished by the injection of prostigmin—a striking support for the contention that the condition is myasthenic in nature. Full details of these experiments have not as yet been published.

(4) *Implantation of Thymic Tissue*.—Multiple implants of thymic tissue into successive generations of rats seem to have the same effect, but to a less degree, as multiple injections of thymus extract into successive generations.<sup>58, 59</sup> By repeated transplantation of young thymic tissue into dogs, Adler states that the same myasthenic condition is produced as by injection of thymic extracts.<sup>23</sup>

As has been stated, it is difficult to evaluate the effects of therapeutic procedures in myasthenia gravis because of the presence of a tendency to spontaneous remissions. Kennedy and Moersch<sup>60</sup> report 87 patients with myasthenia gravis observed at the Mayo Clinic between 1915 and 1932. Of the 84 patients whose subsequent course could be traced, 34 were dead at the time of the report (1937). In 24 of these, death was attributed to myasthenia gravis. Of the remaining 50 patients, 13 reported their condition unchanged, ten were improved, and eight were worse. The condition of seven patients had fluctuated greatly, and the answer to the questionnaire was unintelligible in 13 instances. Regarding remissions, Kennedy and Moersch state: "In 44 of the cases, no mention was made of a remission, and in three other cases the patients failed to reply to the questionnaires. Twenty-seven patients had 43 complete remissions, which ranged from more than one month to 15 years in duration. The average duration of a complete remission was two and two-tenths years; the majority of them lasted less than one year. Thirteen patients had 17 partial remissions which lasted from less than one to 16 years, the average duration being one and five-tenths years. The majority of these remissions lasted less than six months." Other citations from the literature would only serve to substantiate the point that the course of patients with myasthenia gravis varies greatly. It is generally believed that remissions become shorter in duration as the disease advances. If this is true, it lends greater significance to the possible effect of surgical treatment in our patient since she had experienced increasingly severe attacks during the four-year period preceding operation.

The value of roentgenotherapy of the thymic region in myasthenia gravis is open to question. Pierchella<sup>61</sup> reported improvement following irradiation of a patient with hyperplasia of the thymus and myasthenia gravis. Mella<sup>62</sup> noted improvement in one of his patients following irradiation of the thymus. Keschner and Strauss<sup>63</sup> reported disappearance of the shadow in the mediastinum and a remission in the symptoms following roentgenotherapy. Hyland<sup>64</sup>



noted improvement in two of four patients with myasthenia but without demonstrable thymic lesions following irradiation of the thymic region. On the other hand, some observers have noted no improvement following roentgenotherapy. It is difficult to evaluate the effect of irradiation in our patient. It is known that thymic tumors usually are sensitive to irradiation. The degenerative changes which were present in the tumor in our case strongly suggest that the lesion was affected by roentgenotherapy.

It is our impression that our patient would have died during the severe exacerbation of the disease in the early part of 1936, had prostigmin not been available. As has been stated, operation was postponed until a remission occurred. It is likely that the beneficial effects produced by prostigmin will greatly decrease the dangers associated with surgical operations on individuals with myasthenia gravis. If it is decided in the future that surgical exploration of the thymic region is indicated in patients with this disease, it should be performed through an approach which gives adequate exposure, such as division of the upper part of the sternum. One should not rely upon the imperfect view which is obtained through an incision in the lower part of the neck.

In concluding, we wish to emphasize again the absence of conclusive proof that the improvement noted in our patient is due to the removal of the tumor from the thymic region. It is well known that hypertrophy of the thymus may occur without an associated myasthenic state. It will be necessary to have additional clinical tests before this form of therapy can be accurately evaluated. It is possible that additional experience will show that exploration of the thymic region is indicated in all patients with severe myasthenia gravis. This is particularly apt to be true in those patients with tumors that are not sensitive to irradiation.

#### SUMMARY

Fifty-three proven instances of myasthenia gravis associated with abnormalities of the thymus have been collected from the literature. This represents approximately one-half of the cases of myasthenia gravis in which postmortem examinations or the findings at operation have been reported. The removal of a tumor from the thymic region of a patient with myasthenia gravis is described. The greatly improved status of the patient during the three years since operation is recorded. This experience may indicate the advisability of the surgical removal of clinically demonstrable thymic tumors in patients with myasthenia gravis.

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DISCUSSION.—DR. ROY D. McCLURE (Detroit, Mich.): A gland, to be called a gland, surely should have a secretion either internally or through ducts. A study of the embryologic development of the thymus suggests that it should be classified as a gland because its origin is similar to that of the thyroid and parathyroid. Much work has been done in an effort to prove that the thymus is truly a gland, and there have been many shipwrecks among those who have tried to prove that it has a function.

Doctor Blalock has kindly called attention to the work that Doctor Edwards Park and I had done. This was inspired by the work of the Germans, Kloss and Vogt, who had obtained a picture of rickets in their early thymectomized dogs. Their results, in 1914, seemed so specific and so striking that we were impelled to repeat their work. Others had obtained similar results. Park and I failed to get any effect from careful, complete, early thymectomies in dogs. I remember our talking at the lunch table at Hopkins one day about this subject before two of our German exchange doctors. Our animals, which we kept in free runways in the country with a carekeeper, were in excellent shape; you could not tell the difference between the controls and our animals with complete early thymectomy. One of these foreign doctors was the son of a famous German professor of medicine. We were talking of our failure in getting results. He said, "You must go to Germany and see where you make your mistake." It happened that one of our assistants, Dr. Henry Cave, was going to Germany that year and he was very glad to visit Kloss and Vogt. When he came back, he told us of their animals, which were confined in small cages in a dark cellar, and that their diets were inadequate. It was obvious, therefore, that the experimental results which they had obtained were on the basis of diet deficiency.

One day, while I was Resident Surgeon at the Johns Hopkins Hospital, Doctor Halsted, who had authorized and encouraged our experimental work, became (for him) greatly excited over an article published by von Haberer, reporting a series of exophthalmic goiter cases which had not been cured by operation. Von Haberer had recalled one of these cases, and had removed the thymus gland which, as we know, is so greatly enlarged in this disease. That patient got well. Immediately we recalled, for Doctor Halsted, all the cases of exophthalmus which had not recovered. They were all given roentgenotherapy and some of them had a partial thymectomy. I believe none of them were much benefited, to our great disappointment.

Then along came the work of Doctor Rowntree, and his amazing growth-results in the second and third generations of rats. We followed his work with great interest, because it looked as if, at last, he had found an internal secretion of the thymus. But now, even he admits that this result is due perhaps not to the thymus gland but to glutathione, which has a very high content of amino-acid with sulphur (that is cystine and glycine), for by feeding glutathione he can get the same results that he obtained by feeding thymus. The problem, therefore, appears to be far from being solved.

This report of Doctor Blalock's is so striking that time and further similar cases can alone clear this up. We have had ten cases of thymic tumor at the Henry Ford Hospital, but none of them associated with myasthenia gravis. However, it certainly behooves us all to look up our cases, both of myasthenia

gravis and of tumors of the thymus, and see if we can possibly help to clear up this subject.

DR. GEORGE J. HEUER (New York): Doctor Blalock, again, has raised the interesting question of the relationship between myasthenia gravis and pathologic conditions of the thymus gland. His patient, whom we have had the opportunity of seeing, supports the view that there exists a relationship between myasthenia gravis and certain tumors of the thymus. My own interest in the matter dates back many years, when I had the opportunity of studying, on Doctor Halsted's service, a patient with marked exophthalmic goiter who also had symptoms and signs of myasthenia gravis. It was at a time when, particularly abroad, the relationship between the thyroid and thymus in exophthalmic goiter was being emphasized and we were inclined to attribute the manifestations of myasthenia gravis to disease of the thymus gland. About 1930, I collected all the malignant tumors of the thymus gland reported in the literature, finding at that time 85 to 90 cases. I did not find any cases of malignant tumor of the thymus gland in which myasthenia gravis was stated to have been present; but it should be said that in many of the reports specific comments on the presence or absence of this condition are not made.

Dr. N. C. Foot, in his own experience, and in his survey of the literature, failed to find an association between malignant tumors of the thymus and myasthenia gravis. On the other hand, necropsies in patients dying with myasthenia gravis have shown, in about 50 per cent of the cases, a benign enlargement of the thymus; according to descriptions given, a benign hyperplasia, a circumscribed benign tumor or a diffuse benign tumor. As between the circumscribed enucleable tumors and the diffuse tumors, it is my impression that it has been in the former, as in Doctor Blalock's case, that myasthenia gravis has been particularly associated. It is possible, although not yet established, that a particular type of thymic tumor is associated with myasthenia gravis. All cases of thymic enlargement associated with myasthenia gravis should, therefore, be most carefully studied in the hope of clarifying what is now an obscure relationship.

DR. PETER HEINBECKER (St. Louis): I am glad that Doctor Blalock stressed the fact that myasthenia gravis is a disease which is characterized by exacerbation and remissions. These exacerbations and remissions are especially likely to occur at the time of puberty or during pregnancy. They may be precipitated by almost any cause. Also, they are not infrequently of long duration.

Now, as to the underlying mechanism in myasthenia gravis, I am doubtful that it is a weakness of the myoneural junction. I think it is an inability of the muscle to build up quickly the state or materials necessary for a muscular contraction. This statement is based on an examination I made a couple of years ago in a case of myasthenia gravis. I carried out a nerve muscle biopsy and stimulated the nerve about 100 times a second, observing its activity for two hours with a cathode ray oscillograph. It acted in a perfectly normal manner. I stimulated the excised muscle with an electrical current. The first responses were normal and then gradually fatigue set in. If the muscle was allowed to rest, it again contracted normally, soon once more to fatigue. When one stimulates the muscle directly with an electrical current it is not necessary to assume the participation of the myoneural junction in the excitatory process. The contractile process of the muscle is defective. I do not believe that any experimental evidence has indicated that an excess of thymus hormone interferes with the processes of muscular contraction.

## LEFT SUBPHRENIC ABSCESS\*

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MUCH has been written on the subject of subphrenic abscess and many excellent articles are available dealing with the difficulties of its differential diagnosis, its high mortality and the various methods of drainage of such abscesses. Throughout such articles one finds, however, little on the subject of the *left* subphrenic abscess, all of the emphasis being placed on those which occur on the right side. This is due, in all probability, to the fact that subphrenic abscess occurs more frequently on the right side; for example Ochsner,<sup>1</sup> in reviewing 1,517 cases of subphrenic abscess, found that only 412 were on the left, or one abscess on the left to three on the right. Table I, based on some of the more recent literature, indicates that the ratio is about three abscesses on the right side to one on the left. In spite of the fact that subphrenic abscesses occur once on the left for every three or four times on the right, the occurrence of a left subphrenic abscess is not often thought of when the surgeon considers the possibility of a subphrenic abscess in a given case. He is quite apt to feel, after he has ruled out the presence of pus beneath the right half of the diaphragm, that he can entirely dismiss from his consideration the presence of a subphrenic abscess. The old adage "pus somewhere, pus nowhere, pus under the diaphragm" is certainly an excellent one, but should be modified to "pus somewhere, pus nowhere, pus not under the right half of the diaphragm, pus under the left half of the diaphragm." It is frequently stated, and rightly so, that one of the most important aids in making a correct diagnosis of subphrenic abscess is first of all to bear in mind its possible occurrence. The diagnosis is missed or long delayed in practically all abscesses occurring beneath the left half of the diaphragm because, though the occurrence of a subphrenic abscess is considered, its possible location on the left side is rarely kept in mind. To most surgeons "subphrenic abscess" really means "right subphrenic abscess."

*Anatomy.*—In 1908, Barnard<sup>2</sup> gave a very accurate description of the anatomy of the subdiaphragmatic space, and his splendid article is referred to by nearly all of the subsequent writers on the subject of subphrenic abscess. Recently Alton Ochsner has given an excellent description of this area, also, which is a modification of Barnard's. Three subdiaphragmatic spaces on the left side were described by Barnard and it is proposed to follow his terminology in this communication. The spaces are: (1) The left anterior intraperitoneal; (2) the left posterior intraperitoneal; and (3) the left extraperitoneal. The *left anterior intraperitoneal space*, which is likewise

\* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.



# LEFT SUBPHRENIC ABSCESS

TABLE I

ANALYSES OF SUBPHRENIC ABSCESSES PREVIOUSLY REPORTED

Author	Total Cases Reported	Number on the Left Side	Location of Left-Sided Abscesses		
			Anterior Intraperitoneal	Posterior Intraperitoneal	Extra-peritoneal
Ochsner and Graves <sup>1</sup> (own series)	50	5	5	0	0
Overholt <sup>10</sup>	25	2	2	0	0
Schwartz <sup>4</sup>	9	2	2		
Fifield and Love <sup>5</sup>	78	22	14	7	1
McNamee <sup>16</sup>	9	3	3		
Pancoast <sup>19</sup>	16	3	2		1
Gatewood <sup>6</sup>	41	9	Not localized as to space		
Barnard <sup>2</sup>	83	33	30	3	
Gogol <sup>9</sup>	50	0	0	0	0
Beye <sup>8</sup>	23	6	Not localized as to space		
Delario <sup>18</sup>	7	1	1		
Lockwood <sup>3</sup>	82	23	12	8	3
Totals	473	109	71	18	5

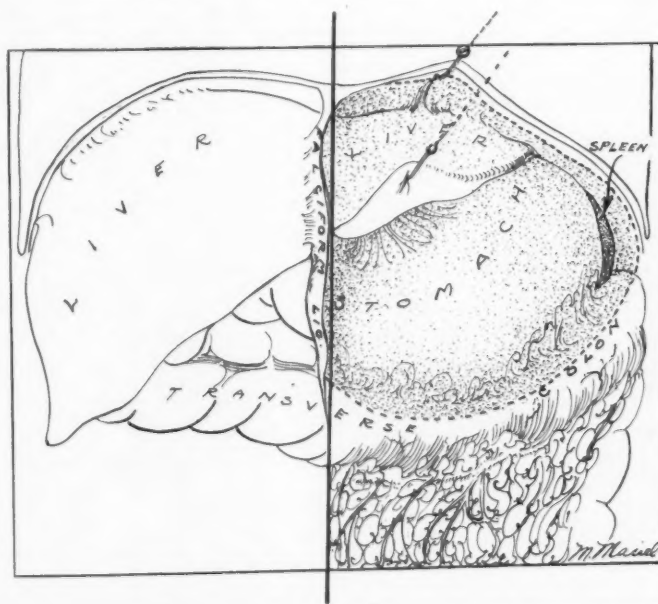


FIG. 1.—The anatomy of left anterior intraperitoneal abscess. The abscess is represented by the dotted area. The transverse colon adherent to the anterior abdominal wall is shown limiting the abscess below.

called the perigastric or perisplenic space, has the following boundaries: The diaphragm above, the left lobe of the liver below and to the right, the spleen to the left, the coronary and falciform ligaments to the right, the left lateral ligament behind and the adhesions between the stomach or the omentum to

the anterior abdominal wall below (Figs. 1, 2 and 3). Although the boundaries of the entire left anterior intraperitoneal space are those just given, the abscess occupying it may not extend to these limits, but may be localized to smaller areas by the formation of adhesions within the space. For instance,

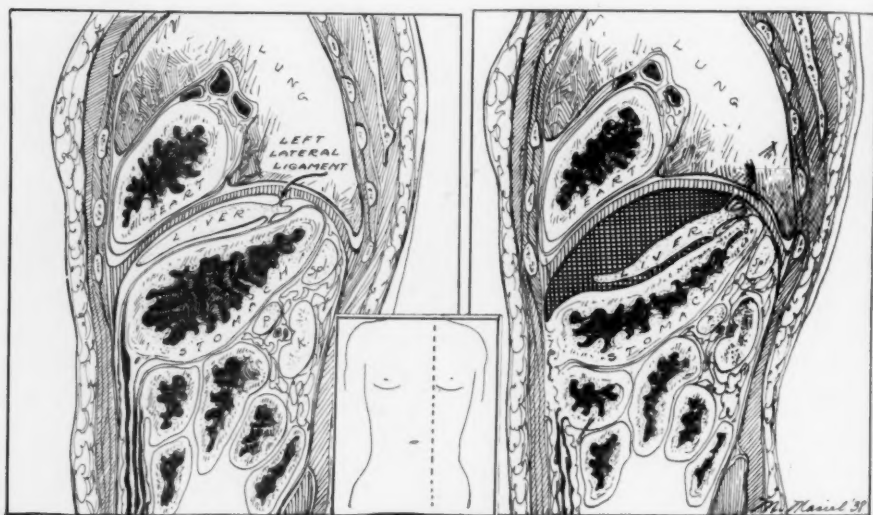


FIG. 2.—The anatomy of a left anterior intraperitoneal subphrenic abscess in the parasternal line. A normal section is shown on the left. Note that the left lateral ligament of the liver forms the posterior boundary of the abscess at this level. The stomach, by adhering to the anterior abdominal wall, has limited the abscess below so that the abscess barely presents below the costal margin.

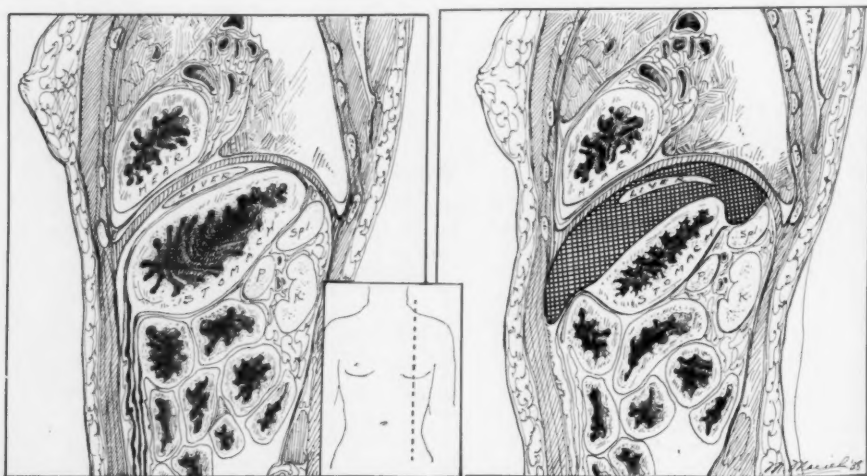


FIG. 3.—The anatomy of a left anterior intraperitoneal subphrenic abscess in the nipple line. A normal section is shown on the left. At this level the spleen limits the abscess behind and somewhat laterally. The omentum has become adherent to the abdominal wall below and forms the lower boundary of the abscess so that a considerable portion of the abscess presents below the costal margin. (Cf. Fig. 2.)

the stomach may adhere to the abdominal wall just at the costal margin and limit the abscess anteriorly (Fig. 2). Whereas, if the colon or mesocolon forms the lower boundary, the abscess will present as a mass in the left upper quadrant (Fig. 3).

## LEFT SUBPHRENIC ABSCESS

The left anterior intraperitoneal space has connections with other spaces and pouches which are important from the point of view of spread of infection from elsewhere *to* this space and spread of pus *from* it to other areas. It connects around the left margin of the liver with the right subhepatic space and below with the left lumbar pouch which lies between the descending colon and the lateral abdominal wall. Barnard described a direct pathway from the pelvis to the left anterior intraperitoneal space (Fig. 4) of which I have found no other mention made, but which is of importance, for it explains why a left subphrenic abscess so frequently follows suppuration in the pelvis.

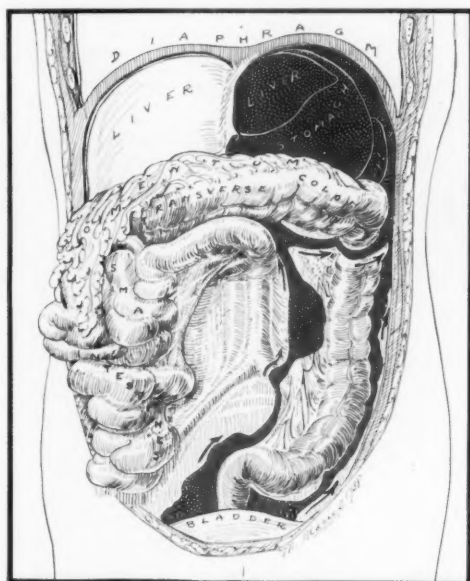


FIG. 4.—The pathways by which pus spreads from the pelvis to the left subphrenic space. The lumbar pouch is shown to the outside of the descending colon and the route described by Barnard<sup>2</sup> to the inside, with the spine forming the medial boundary up to the duodenojejunal flexure at which point the pus is directed around the left edge of the splenic flexure into the left anterior intraperitoneal space.

This pathway leads from the rectovesical or recto-uterine pouch over the left sacro-iliac joint to the gutter formed by the vertebral column on the right, the descending colon on the left and the mesentery behind. This gutter directs the pus up to the duodenaljejunal flexure whence it passes forward along the splenic flexure to reach the left anterior intraperitoneal subphrenic space. Barnard states that a "trail of pus" can be found along this route in many cases of pelvic peritonitis. Pus may also reach the left subphrenic space from the pelvis by flowing along the left lumbar pouch, *i.e.*, between the colon medially and the lateral abdominal wall laterally (Fig. 4). With the patient in a recumbent position, it can readily be seen how pus could spill out of the pelvis and be directed by one of these two routes to the left subphrenic space. In five of the six cases herewith reported, there was pus in

the pelvis before the development of a left subphrenic abscess, namely, three cases of postpartum infection, one of a localized pelvic abscess ("which disappeared suddenly") and one of a pelvic appendix which had ruptured, filling the true pelvis with thick pus.

The *left posterior intraperitoneal space* is in reality the lesser peritoneal sac. This space is primarily infected by the perforation of a gastric ulcer or carcinoma situated on the posterior aspect of the stomach. It may be secondarily infected by pus entering the foramen of Winslow, usually from a right subhepatic abscess.

The *left extraperitoneal space* is the loose areolar tissue which surrounds

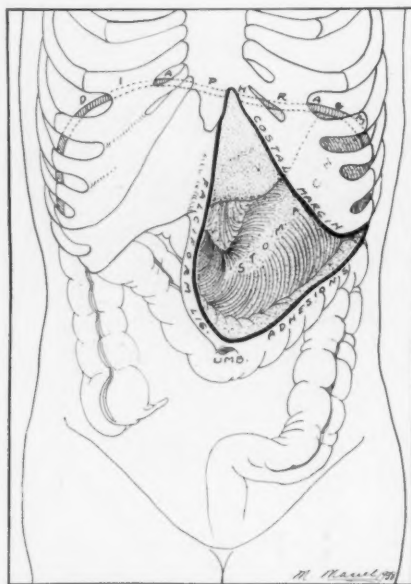


FIG. 5.—The triangular area of fulness and tenderness which is present in the type of large left subphrenic abscess when the transverse colon forms the lower limit of the abscess, and the falciform ligament the right boundary.

the kidney, the pancreas and the descending colon on its posterior aspect. It is very rarely infected. Cases of abscess in this area have been reported by Barnard as following an infection of the vertebral bodies, a long standing chronic empyema and a stomach ulcer which had perforated posteriorly. Clinically, such abscesses point in the lumbar region and simulate the perirenal abscesses.

Of the three spaces described, the most important is the *left anterior intraperitoneal*, chiefly because it is the most frequently infected.

*Signs and Symptoms.*—The diagnosis by physical examination of an abscess beneath the left leaf of the diaphragm is even more difficult than it is when the abscess lies beneath the right half of the diaphragm, for such an abscess gives fewer physical signs of its presence. On the right, the firm,

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large right lobe of the liver forms the floor of the abscess, whereas, on the left, there is little liver substance, but the abscess is encompassed below by more yielding structures, such as stomach, falciform ligament, colon, spleen and transverse mesocolon. Consequently, on the left there is apt to be less bulging in the lower thorax and costal margin, less restriction of movement of the lower portion of the thoracic cage, less local pain because of less tension of the pus and less elevation and fixation of the diaphragm itself. It is true, however, that in the case of the left anterior intraperitoneal abscess (most common variety) tenderness on pressure beneath the costal margin can be elicited earlier and more definitely than on the right, and when it reaches a large size it may actually be felt as an indefinite mass below the left costal margin. If the whole space is filled with pus one can outline a characteristic triangular mass described by Barnard as extending from under

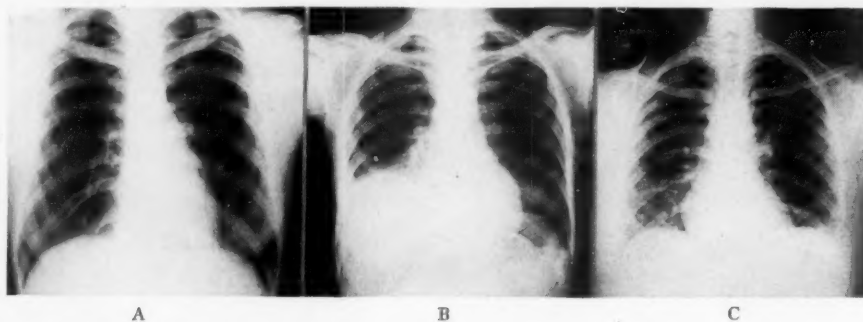


FIG. 6.—(A) Normal relationship between the right and left halves of the diaphragm. (B) The relationship between the two halves of the diaphragm in a case of right subphrenic abscess. The elevation of the right half of the diaphragm is very evident. (C) The relationship between the right and left halves of the diaphragm in a case of left subphrenic abscess. The elevation of the left half of the diaphragm is scarcely noticeable.

the left costal margin to a line from umbilicus to costal margin and from ensiform cartilage to umbilicus (Fig. 5). Pain referred to the shoulder and neck is greater with left-sided abscesses because of the less fixed diaphragm, the movement of which against the abscess causes the pain to be referred to the neck. In five of the six cases reported herewith, severe pain in the left lower thorax and in the neck was a prominent symptom. Owing to the fact that the abscesses which occur on the left side are apt to be diagnosed late, the so-called "thoracic signs" are more commonly seen than in the case of right-sided abscess. These signs are "fuzziness" of the diaphragm on the roentgenogram, those of pneumonitis, or those of fluid (serous or purulent) of varying amount in the pleural cavity. In fact, it is only too often the signs of fluid in the left pleural cavity, which is secondary to the abscess, that bring about the diagnosis of the abscess itself. Such was the case in two instances in the series reported here. It is most essential to bear in mind that fluid above the diaphragm frequently means pus below it and to suspect the abdomen rather than the chest.

*Roentgenologic and Fluoroscopic Examination.*—The roentgenogram and



the fluoroscope are probably the most useful aids in establishing a diagnosis of subphrenic abscess. Examination under the fluoroscope characteristically shows a high, fixed diaphragm in the case of right-sided abscess. With the left-sided abscess, however, the diaphragm is not so high for the reasons given above. Even if it is high, the discrepancy of its height as compared to that on the right is not so noticeable, since it normally is lower than the right, or its elevation may be attributed to abdominal or gastric distention, both of which influence the left half of the diaphragm more than the right (Fig. 6). On the left, however, fixation of the diaphragm is a most important sign of an abscess beneath it, and it occurs even though the diaphragm is not high. The presence on a roentgenogram of an air bubble beneath the *right* half of

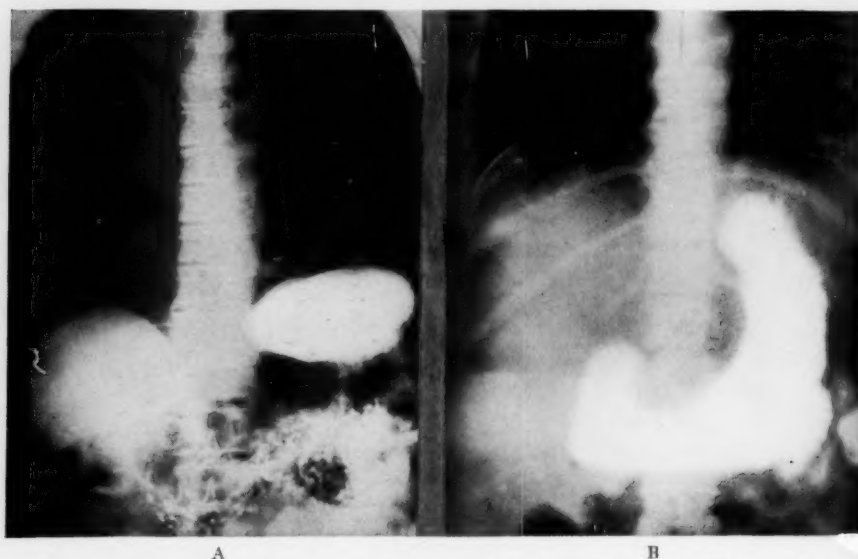


FIG. 7.—Roentgenograms showing (A) the normal relationship of the barium filled stomach to the diaphragm; and (B) the downward and medial displacement of the stomach by the subphrenic abscess in Case 4.

the diaphragm with a fluid level beneath it clinches the diagnosis of subphrenic abscess. This finding is said to occur in from one-fourth to one-half of the cases of subphrenic abscess and can be detected if films are taken from various angles. Air and fluid beneath the right half of the diaphragm are easy to detect, but beneath the left half, confusion is caused by the normal findings of air and fluid in the stomach. Consequently, the fluid level and air in a subphrenic abscess are easily overlooked on the left side. The true nature of such air can be very easily determined by the simple expedient of filling the stomach with barium. Normally the stomach, when filled with barium and with the patient in a low Trendelenburg position, lies in contact with the diaphragm (Figs. 7 and 8). If there is an abscess beneath the diaphragm, the barium-filled stomach will be found to be separated from the undersurface of the diaphragm by a considerable space which may contain air or may not. Even if there is no air in a left subdiaphragmatic abscess, the filling of the

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stomach with barium will establish the diagnosis, owing to the displacement of the stomach downward and medially and posteriorly by the abscess if it lies in the anterior space, or anteriorly if the abscess lies in the posterior space (Figs. 7 and 8). After being given the barium by mouth, the patient should be placed in a low Trendelenburg position to insure that the stomach comes in contact with the diaphragm, if it is possible for it to do so. By this one simple maneuver, the diagnosis of left subphrenic abscess becomes a much simpler and easier matter, yet I can find no reference to its use in the surgical literature. It should be used whenever there is a suspicion of a left subphrenic abscess.

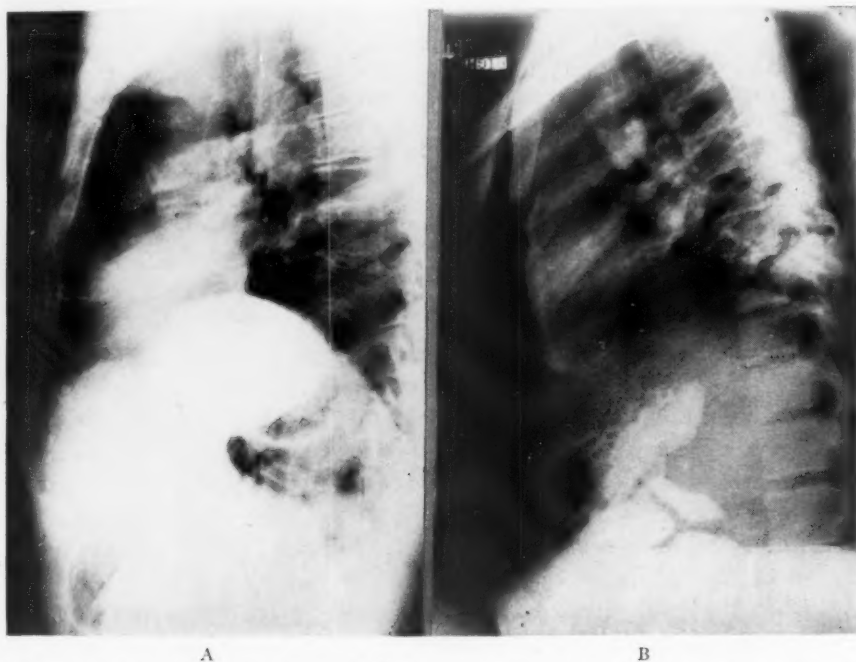


FIG. 8.—Lateral roentgenograms showing (A) the normal relationship of stomach to diaphragm; and (B) the downward displacement of the stomach by the subphrenic abscess in Case 4.

### CASE REPORTS

**Case 1.**—Hosp., No. 5758G: F. L., female, age 19, was admitted to the Good Samaritan Hospital, August 21, 1935, complaining of weakness and pain in the left upper quadrant and lumbar region. Her past history was of no importance. Her present illness began in November, 1934, when, after having been delivered of a normal child, she contracted a postpartum infection to which she nearly succumbed. She was confined to bed in another hospital from the time of delivery until February 20, 1935. After being at home and in bed for three months she began to be up and about. During this time she ran a low-grade fever, felt weak and sick and had a soreness and pain in her left lower chest and upper abdomen. These symptoms became more acute in August, 1935, when she was admitted to the Good Samaritan Hospital in care of Dr. F. Williams and Dr. Clyde Roof. It was found that she had been having severe knife-like pains in the upper left quadrant and a sharp pain referred to her left shoulder, that there had been occasional attacks of vomiting

and a feeling of weakness and lassitude. Her temperature ranged between 98° and 100° F., pulse 100, respirations 20. W.B.C. 10,375; R.B.C. 3,700,000; Hb. 72 per cent.

*Physical Examination.*—There was lagging of the left costal border with some fullness, dullness at the left base and very little excursion of the diaphragm. Roentgenologic examination of the chest showed a high diaphragm on the left with no fluid in the pleural cavity and the lungs clear. Fluoroscopic examination revealed that the left diaphragm was high and fixed and that there was an air space with a fluid level just beneath the diaphragm. Barium was given by mouth and films taken with the patient lying flat on the table. These showed that the true air bubble in the stomach was separated from the air space referred to above by a considerable distance. From these examinations it was obvious that one was dealing with a left subphrenic abscess. A barium enema was given, and some of the barium was found to enter the abscess cavity. It was clear now that the subphrenic abscess communicated with the transverse colon, having ruptured into it at some previous time.

*Operation.*—September 3, 1935, Doctor Roof: Nitrous oxide-ether anesthesia. Suspecting that there might be difficulty in localizing the abscess, a short, high, left rectus incision was made, and the abscess located beneath the costal margin. A short segment of rib in the midaxillary line was resected. A rubber tube and cigarette drains were inserted. The abscess cavity, which was about 10 cm. in diameter, lay between the anterior portion of the diaphragm and the undersurface of the liver above and the transverse colon and spleen below, and was bounded posteriorly by the stomach—in other words, it was a left anterior inferior subphrenic abscess.

The wound drained feces and pus for two weeks and then rapidly healed. The patient was discharged, September 20, 1935. She was readmitted, November 6, 1936, at which time her right tube, ovary and appendix were removed. Since then she has remained well.

*COMMENT.*—The diagnosis in this case was made nine months after the onset of a postpartum infection, which seems to have been the logical cause for the subphrenic abscess. It is impossible from the history to determine when the abscess ruptured into the colon, but from its small size, when found at operation, and from its thick fibrous walls, the rupture must have occurred many weeks before operation. The repeated episodes of fever and malaise which occurred at intervals during her long illness must have been due to periods of poor drainage of the contents of the abscess into the colon. It is interesting that on fluoroscopic examination an air bubble was seen beneath the left diaphragm, but one could not be sure whether the air bubble was in the stomach or not until the barium was given. Barnard reports spontaneous rupture of 23 subphrenic abscesses, occurring into the bronchus in four cases, into the pleura in five cases, into the stomach in eight cases, into the colon in two cases, through the skin in two cases, into the peritoneal cavity in one case and into the small intestine in one case.

*Case 2.*—Hosp. No. 101749: J. L. E., white, male, age 31, was admitted to Christ Hospital, March 12, 1936, with a diagnosis of "a ruptured appendix with peritonitis." He was operated upon immediately by Dr. E. A. Kindel. Through a McBurney incision, a ruptured gangrenous, pelvic appendix was removed, a colon bacillus and Staphylococcus peritonitis found and cigarette drains were placed into the pelvis and down to the cecum (a large fecalith had been removed from the pelvis.) After a stormy convalescence for four days, he began to improve considerably, but ten days after operation, he began to complain of pain in the left lower thoracic region and on examination signs of fluid were detected in the left chest. The left pleural cavity was aspirated, March 24, 1936, 12 days after operation, and 10 cc. of yellow, cloudy fluid was obtained, which was negative

## LEFT SUBPHRENIC ABSCESS

for organisms on smear and culture. A roentgenogram of the chest, March 27, showed "fluid in the left chest." On April 1, 700 cc. of fluid of the same character was removed from the left pleural cavity, and on April 9, 28 days after operation, 600 cc. of frank pus with a fecal odor was withdrawn. On the following day, a closed aspiration drainage was established in the left pleural cavity. At this time the patient appeared extremely toxic, slightly jaundiced, the tube in the left chest was functioning well, the abdomen was moderately distended and a large tender mass in the region of the right lobe of the liver was made out.

*Operation.*—April 11, 1936, Doctors Kindel and Carter: There was a good deal of bile-stained fluid in the peritoneal cavity. The right lobe of the liver was very large and bulging; it was opened and an abscess containing about 1,000 cc. of bile-stained pus and inspissated bile was evacuated. After removal of the pus, a large cavity remained, which we took to be in the liver, and from which a prolongation extended far up toward the left lobe. The edges of the opening in the liver were sutured to the peritoneum and the rest of the wound loosely closed after soft rubber tubes and cigarette drains had been placed into the abscess cavity.

The abdominal wound drained large quantities of bile-stained pus and bile, and the tube in the left thorax discharged foul-smelling pus. One month after operation, both wounds had ceased to drain, and the patient was discharged. He has remained well since that time. During the convalescence repeated roentgenograms showed a cavity below the diaphragm as well as an empyema cavity above it, so that the diagnosis of left subphrenic abscess was established beyond question.

*COMMENT.*—Ten days after operation, fluid was discovered in the left pleural cavity. This, combined with the pain in the left lower chest, was the first evidence of the left subphrenic abscess and it is probable that the abscess could have been diagnosed at that time had barium been given by mouth and roentgenograms taken with the patient flat on the table or in a slight Trendelenburg position. It is interesting to speculate as to whether the liver abscess was the cause of the left subphrenic abscess, due to its rupturing under the diaphragm, or whether the subphrenic abscess burrowed into the liver as well as through the diaphragm and then caused the liver abscess. The anatomic location of the subphrenic abscess was not definitely determined.

*Case 3.*—Hosp. No. 79071: F. J., colored, male, age 14, was admitted to the Cincinnati General Hospital, August 28, 1937, with a diagnosis of ruptured appendicitis. He was immediately operated upon, and a gangrenous, ruptured appendix removed. A good deal of odorless, thick fluid was aspirated from the peritoneal cavity and the peritoneum closed tightly, only the wound itself being drained. Six days after operation, a small pelvic abscess was detected, which increased in size until the tenth day, when it suddenly disappeared. Coincident with its disappearance, the patient became acutely ill, with a distended abdomen, high temperature and vomiting; it was felt that the pelvic abscess had ruptured into the peritoneal cavity. Under appropriate treatment the peritonitis subsided within two or three days. On the fourteenth day after operation, the patient complained of pain in the left lower chest—there were signs of fluid in the left chest, both on physical examination and roentgenologically. An aspiration of the left chest was productive of cloudy, straw-colored fluid, which contained a few Cocci and Bacilli. This fluid became frankly purulent within two days, and a closed drainage was established in the left pleural cavity. The tube did not function well on account of the thickness of the pus, so, on September 28, 1937, a four-inch segment of the eighth rib in the midaxillary line was resected and a wide opening made into the empyema cavity. It was immediately obvious that there was a hole through the diaphragm leading into a left subphrenic abscess. Up until this time, there had been no mention made of the possibility of such

an abscess being present. The opening in the diaphragm was enlarged by excising a portion of it. A large, soft rubber tube was placed in the cavity and the wound left open. Lipiodol was injected into the sinus and the subphrenic abscess well demonstrated, it was a *left anterior intraperitoneal* abscess. This patient developed a large pelvic abscess and a large intra-abdominal abscess in the region of the McBurney incision. Both of these were drained and the remainder of the convalescence was smooth, the patient being discharged "well" but rather badly battle scarred, December 1, 1937. He has remained well since.

COMMENT.—The diagnosis of a left subphrenic abscess was not made in this case until after an empyema cavity had been widely opened and the opening through the diaphragm actually seen. A "subphrenic abscess" (meaning a right subphrenic abscess) had been thought of and ruled out by repeated fluoroscopic examinations. The diagnosis of left subphrenic abscess was missed because *it was not considered*. Had it been thought of, the correct diagnosis could have been made when the first complaint of pain in the left chest was mentioned.

Case 4.—Hosp. No. 86564: L. J., colored, female, age 42, was admitted to the Cincinnati General Hospital, January 27, 1938. She was a very obese woman who was eight months pregnant and was suffering from early antepartum eclampsia. Blood pressure 226/150. She was dyspneic, had edema of the lower half of her body, and a temperature ranging up to 103° F. Her membranes ruptured spontaneously and after the introduction of a Braun bag she was delivered of a macerated fetus by version and extraction, the placenta being removed manually. Following delivery, she developed a puerperal sepsis with signs of peritonitis and nonhemolytic Streptococci in her blood stream. Large doses of sulfanilamide were given together with two transfusions. The blood culture became negative, the blood pressure fell to 120/70 and the peritonitis subsided. One month after admission, she was running a temperature up to 100.4° F., the abdomen was soft and not tender. An abscess of the buttock was drained, March 1, and the temperature fell to 99° F. On March 10, she began to complain of sharp, cutting pains in the lower left chest. The pain continued, increased in severity, and she began to have sharp pains on inspiration referred to her left shoulder.

Diaphragmatic pleurisy was suspected, and a fluoroscopic examination was made, March 12. This revealed a fixed diaphragm on the left, the two crura being on the same level. On March 18, the patient had a severe chill and the temperature rose to 103° F. On March 24, she vomited several times, complained of generalized abdominal pains, became distended and had generalized tenderness over the whole abdomen. She was seen by the Surgical Service, March 24. At that time, there were signs of a generalized peritonitis and a suggestive mass could be felt below the left costal margin. A diagnosis was made of left subphrenic abscess with rupture and resulting peritonitis. Fluoroscopic examination on that day showed the left diaphragm to be fixed and to be "slightly" elevated. A roentgenogram, made after a barium meal, showed the *fundus of the stomach displaced downward and medially*.

Operation.—Under local anesthesia, a four-inch segment of the ninth rib was resected in the left midaxillary line. The parietal pleura was edematous and firmly adherent to the diaphragm; the diaphragm was, therefore, opened widely and an abscess containing about 200 cc. of thin, foul pus was found beneath it. The abscess lay anteriorly and extended forward to the costal margin and laterally to the spleen. It was an *anterior intraperitoneal subphrenic* abscess. Two large, soft rubber tubes were inserted and the wound left open. Her postoperative course was stormy. The signs of peritonitis continued and a mass appeared in the upper right quadrant. On April 9, an incision was made over this mass and 120 cc. of thin, foul pus evacuated. Pus was seen to well up



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from between loops of bowel near the collection of pus noted above. The patient died seven hours after the operation. No autopsy could be obtained.

**COMMENT.**—The symptoms of pain in the lower left chest and pain referred to the left neck and shoulder appeared six weeks after the postpartum infection, and at that time a fluoroscopic examination was made. It is significant that though the report stated that the left diaphragm was fixed and on the same level as the right, it made little impression on the attending physicians. If the right diaphragm had been correspondingly as high as the left really was, I venture to say that the diagnosis of right subphrenic abscess would have been made at once. The correct diagnosis was made by the single expedient of a barium meal followed by a roentgenogram taken in a slight Trendelenburg position, but only after the abscess had ruptured with the production of a fatal peritonitis.

**Case 5.**—Hosp. No. 93036: E. T., white, male, age 53, was admitted to the Cincinnati General Hospital, April 15, 1938, one and one-half hours after having been stabbed in the abdomen. He was in mild shock, quite drunk, and difficult to manage. There were two stab wounds through the abdominal wall, one below and to the right of the umbilicus, and one at the outer edge of the left rectus muscle just below the costal margin. He persisted in refusing to be operated upon throughout his stay in the hospital. He was treated with a continuous Wangensteen drainage, a blood transfusion of 300 cc. daily for eight days, morphia, and was placed in Fowler's position. He lived for ten days, and died with all the signs of sepsis and peritonitis. On the fifth day of his illness, he began to show some dullness at the left base with limitation of the movements of the left half of the diaphragm. A fluoroscopic examination, made on the eighth day, showed a fixed, high diaphragm on the left, but no barium was given by mouth on account of the patient's abdominal condition. An autopsy was obtained.

**Autopsy.**—There was an old generalized peritonitis, fibrinous in character, two ragged holes in the ileum, which were sealed-off against the anterior abdominal wall, and an abscess holding 500 cc. of pus beneath the left diaphragm. This abscess was bounded by the diaphragm above, by the right lobe of the liver and stomach medially and inferiorly by the spleen and transverse colon.

**COMMENT.**—The correct diagnosis of left subphrenic abscess was advanced in this case, and was based upon pain in the left lower chest, limitation of motion of the left costal margin, and a fluoroscopic finding of a high, fixed diaphragm. Barium could not be given by mouth due to the perforation in the intestine.

**Case 6.**—Hosp. No. 99578: A. B., white, female, age 29, was admitted to the Cincinnati General Hospital, July 6, 1938, with a diagnosis of incomplete abortion. A curettage was performed, the convalescence was smooth and the patient was discharged at the end of 12 days, apparently well. She was readmitted, however, 12 days later with an obvious general peritonitis and was desperately ill for five days, after which she showed satisfactory improvement for six days. During this time, she had received three blood transfusions, adequate doses of sulfanilamide, continuous gastric drainage and copious amounts of fluids by vein. On the fourteenth day of her second admission, her temperature rose to 103° F. and she complained bitterly of pain in the left shoulder and neck, the pain being increased on deep inspiration. There was tenderness over the left trapezius muscle. A left subphrenic abscess was suspected, and this diagnosis was substantiated by finding a high, fixed diaphragm on the left side on fluoroscopic examination, and by demonstrating downward and medial displacement of the barium-filled stomach. A two-

stage transpleural approach was made at the level of the ninth rib in the midaxillary line, and a subphrenic abscess containing 300 cc. of thick *Staphylococcus pus* was evacuated. Her subsequent course was satisfactory, and she was discharged as well, 40 days after operation.

**COMMENT.**—In this instance, the correct diagnosis of left subphrenic abscess was promptly and accurately made. This was largely due to the interest now being taken in this Clinic in this condition. The roentgenogram, taken in the Trendelenburg position, after the ingestion of a barium meal demonstrated the condition very well.

**Treatment.**—The proper treatment of a left subphrenic abscess is adequate drainage as soon as feasible after the diagnosis is made. An abscess lying in the anterior intraperitoneal space is best drained extraperitoneally, through an incision just below the costal margin if it presents anteriorly. If it cannot be palpated below the costal margin, a transpleural approach at the level of the eighth or ninth rib in the midaxillary line should be employed. Abscesses in the lesser peritoneal cavity should be drained through a celiotomy, and by an opening in the transverse mesocolon or gastrohepatic omentum, depending upon where the abscess is presenting. Extraperitoneal abscesses may be drained by an incision in the lumbar region directly over them.

One of the six patients in this series refused operation; two of the six patients had their abscesses drained through a transpleural approach, one through the transperitoneal route and in two others the subphrenic abscess, which had ruptured through the diaphragm, was drained at the time of the thoracotomy for the empyema.

#### CONCLUSIONS

(1) The occurrence of subphrenic abscess on the left side has not been emphasized enough heretofore; most of the attention has been directed to the right-sided abscess. Statistics indicate that, of every four or five subphrenic abscesses, one will be on the left side.

(2) Subphrenic abscess on the left is more difficult to diagnose by physical examination than is the right-sided variety.

(3) The roentgenologic and fluoroscopic diagnosis of left subphrenic abscess can be simplified and made more certain by examining the patient after the stomach has been filled with barium.

(4) Six cases of left subphrenic abscess are reported in detail. They emphasize the fact that these abscesses are diagnosed late, and often only then, because of rupture into the pleura, into a hollow viscus or into the peritoneal cavity.

(5) Suppuration in the pelvis, especially postpartum infection, is frequently the cause of left subphrenic abscess.

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DISCUSSION.—DR. ALTON OCHSNER (New Orleans, La.): The Association is indebted to Doctor Carter for calling attention to the relatively frequent occurrence of left-sided subphrenic abscess. I should like to show briefly our modification of Bernard's localization of the subphrenic abscess.

Surgically the subphrenic space is bounded above by the diaphragm and below by the transverse colon and mesocolon. There are three spaces on the right and three on the left. Those on the left, we have divided into two below the liver, the antero-inferior space and a postero-inferior space, which is the lesser peritoneal sac. There is a single space above the liver. That is due to the fact that the left prolongation of the suspensory ligament runs in an oblique angle, extending posteriorly on the left.

About a year ago Doctor DeBailey and I collected 1,531 cases of subphrenic abscesses, and found that 906 of them, or 59 per cent, were on the right side. This included our own cases. Fourteen per cent were retroperitoneal, and 27 per cent, or approximately a fourth, were left-sided. Sixty-eight, or almost 5 per cent, were combined.

To break this down, one finds that of the left-sided abscesses, the left antero-inferior, which is the space which Doctor Carter referred to, is most frequently involved. The left superior, that is, above the liver and between it and the diaphragm, was involved next most frequently, or approximately 4 per cent, and the lesser side in a smaller percentage.

Doctor Carter's diagnostic test is certainly a desirable one because it is

difficult to make a diagnosis of left-sided subphrenic abscesses. Probably the greatest difficulty is not thinking of the possibility.

I do not believe that any patient with a subphrenic abscess should be allowed to develop a pleural effusion. They develop it only because of the delay in the diagnosis.

I want to emphasize the importance of draining subphrenic abscesses extraserously when it can be done. The mortality rate in our series of 36 cases of subphrenic abscess drained extraserously is 6 per cent as contrasted with the mortality rate of most of the reported cases varying from 25 to 75 per cent.

DR. STUART HARRINGTON (Rochester, Minn.): I was very much interested in Doctor Carter's presentation of the subject of left subphrenic diaphragmatic abscess. He has emphasized the difficulties associated with their recognition which often led to a late diagnosis. I was particularly interested in his comment upon the fact that these abscesses occasionally rupture through the diaphragm into the lung and empty into the bronchus. I should like to call attention to a late surgical condition which occasionally results from a rupture of a left subdiaphragmatic abscess through the diaphragm into the lung. The abscess produces inflammatory necrosis of the diaphragm and often produces a large opening through the diaphragmatic muscle at the point where it ruptures into the lung. If the drainage of the abscess is complete, the abscess may heal and later the stomach may herniate through this opening in the diaphragm. This, however, is not a common cause of diaphragmatic hernia; it was the etiologic factor in only three of the 210 cases of diaphragmatic hernia upon which I have operated. The following case is an instance of this type upon which I operated in 1931.

**Case Report.**—The patient was a law student, age 22, who had been taken suddenly ill at night following a banquet, ten months before his admission. He had had severe epigastric pain which had become more or less generalized and his temperature had reached 104° F. Later, pain had developed in the left subphrenic region and vomiting had occurred. Immediate operation had been considered but was not performed because of the diffuse character of the symptoms. The course of the disease remained septic for three weeks. The pain and tenderness then had become localized in the left upper quadrant of the abdomen. Four weeks after the onset, the patient had had a severe attack of coughing during the night, and had coughed up about one quart of pus. A general decrease in the cough and expectoration had occurred during the next two months, with cessation of thoracic and abdominal symptoms. The patient had gained 25 pounds. His condition had gradually improved and all of the abdominal symptoms had disappeared.

He had returned to his work and after about one month pain had developed in the left side of the upper part of the abdomen on taking food. This pain had been referred to the left shoulder; it had not been related to any particular type of food. His breakfast and midday meals had been rather light and he had had little discomfort after these meals. The evening meal had been heavy, and following this he had had most of his trouble. Three months after the onset of these symptoms he had begun to vomit when the stomach was full. This had become progressively more severe and of retention type. He often had vomited large quantities, two quarts at a time, and the vomitus often had contained coffee-ground material. All of his symptoms had been relieved as soon as the stomach had been emptied, or by vomiting.

The roentgenograms of the stomach and esophagus showed elevation and fixation left side of diaphragm; the stomach was fixed to the diaphragm. On reexamination, the same diagnosis was made. Because of his symptoms, which were very suggestive of hernia, operation was advised. Operation disclosed that practically the entire stomach had herniated through a large opening in the left leaf of the diaphragm. There was also

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herniation of three or four feet of the transverse colon. An enormous number of adhesions were present throughout the entire left half of the upper part of the abdomen and the herniated viscera were very adherent to the margins of the opening, which was situated about 2 cm. to the left of the esophageal opening, in the posterior portion of the left half of the diaphragm. The herniated viscera were replaced in the abdomen and the abnormal opening in the diaphragm was closed with interrupted silk sutures and continuous sutures of fascia lata. His convalescence was uneventful and he made a satisfactory recovery.

This case is of particular interest not only because of the infrequency of the occurrence of left subphrenic abscess but also because of the rare occurrence of complete healing of left subphrenic abscess following traumatic rupture through the diaphragm and into the lung. It is also of particular interest because of the occurrence of diaphragmatic hernia through the site of rupture of the abscess through the diaphragm. The clinical evidence was the most important factor in establishing a diagnosis in this case. The roentgenogram before operation did not disclose the presence of a hernia but revealed that the stomach was adherent to the undersurface of the diaphragm and was causing obstruction. This was due to the fixation of the lung around the margins of the diaphragm on the pleural side. The lower margin of the lung gave the appearance of the diaphragm but at the time of operation it was found that the stomach had herniated through the opening and was fixed to the undersurface of the lung rather than to the diaphragm. While this is an infrequent cause of diaphragmatic hernia, I have seen two subsequent incidences, and in these cases the interval between the onset of the acute abdominal condition and the symptoms of the hernia were much greater. In one case, several years had elapsed before the diagnosis of diaphragmatic hernia was established.

DR. EVARTS A. GRAHAM (St. Louis): I wish to add an additional feature to this presentation and also to the discussion of Doctor Ochsner, and that is that occasionally a subphrenic abscess is not limited to a single space such as has been portrayed by the speaker. I am not referring to bilateral subphrenic abscess, but a subphrenic abscess on one side of the body which is not necessarily confined to a single space. For example, not long ago I had a patient with a subphrenic abscess in what Doctor Ochsner would call the left antero-inferior space, from which space I obtained about 500 cc. of pus. He improved somewhat, but did not recover, and it was necessary to operate upon his left postero-inferior space, at which time about 300 cc. of additional pus was obtained, after which the patient made an uneventful recovery.

I have seen at least one other patient, similar to the case cited above, in whom pus was multilocular, that is, occupying more than one space, when it occurred on the left side.

DR. ROSCOE R. GRAHAM (Toronto, Canada): May I express my appreciation for the information so ably presented on this interesting and difficult subject. We have observed, following abdominal operation, upon patients under spinal anesthesia, that postoperative roentgenograms of the abdomen will show that gas is present under the diaphragm for as long as three weeks following operation. The importance of appreciating this fact becomes obvious in a patient who is doing badly following operation, and in whom one might suspect a subphrenic abscess as the cause. Thus, it would be obvious that the presence of a gas bubble under the diaphragm within three weeks post-operative, if the patient had been operated upon under spinal anesthesia, would not be evidence of subdiaphragmatic suppuration. (Lewis, F. I.: J.A.M.A., 28, 18, 1938.)



## EXTRAPLEURAL PNEUMOTHORAX\*

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THE OPERATION of extrapleural pneumothorax has brought a new method to our aid in the treatment of tuberculous cavities in the lung. Although suggested by Tuffier as far back as 1891, and demonstrated as practical in single or small groups of cases by continental surgeons during the past few years, the method did not meet with general acceptance until the reports, in 1937, by Graf<sup>3</sup> and Schmidt,<sup>1</sup> of 107 and 155 cases, respectively. Their low operative mortality and the rapid symptomatic improvement, as well as conversion of the sputum, plus the comparative simplicity of the procedure in suitable cases, brought it into immediate favor.

Recent reports by surgeons of several countries agree as to low mortality and beneficial effect of rapid closure of cavities by selective collapse of the diseased area, but all agree in the necessity of prolonged maintenance of the air-pocket. Therefore, the operation being of so recent origin, not enough time has elapsed for any reports of final results, but, for the reasons already mentioned, and especially the lesser gravity of the operation as compared with thoracoplasty, the general opinion has been, to use the words of Coryllos,<sup>2</sup> "that it is well worth trying."

Also, in recent reports there has been shown a close similarity as to technic with that described by Graf and Schmidt. The adherence to strict indications, however, has evidently not been as close, and the result has been the application to cases which were apparently not suited to the method. It seems, therefore, important for the guidance of those beginning the use of this operation, to report unfavorable results as well as successes, which is the purpose of the present communication.

For the sake of clearness, it may be well to briefly review the indications for this operation and the technic as laid down by the principal writers who have already reported their experiences.

As the name implies, the aim of the operation is to produce a selective collapse of the part of the lung involved, usually the apex, by means of an air-pocket made by stripping the pleural layers off the inner surface of ribs and intercostal muscle sheaths. The production of this extrapleural space causes a collapse of the lung, varying in amount with the extent of the stripping, the maintenance of which depends on two factors: (1) Tight closure of the innermost layer of chest wall tissue to form a complete air sac for compression of the lung; and (2) repeated injections of air into this space for a prolonged period in order to obtain healing of the obliterated cavity. The latter part of the treat-

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\* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

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ment is quite the same as in intrapleural pneumothorax with certain minor differences.

*Indications.*—The indications for the operation as given in more recent articles are as follows:

- (1) Cases with apical cavernous disease with complete pleural symphysis, or apical adhesions too extensive to be dealt with by intrapleural pneumolysis.
- (2) More extensive unilateral disease with pleural symphysis, but whose vital capacity is great enough to tolerate a sudden and extensive collapse. From our own experience we place the minimum at 1,500 cc. in such cases.
- (3) Cases where, owing to concurrent cardiac disease, old age, asthmatic or emphysematous condition, thoracoplasty is contraindicated.
- (4) Growing children where thoracoplasty is undesirable.
- (5) Early stages of the disease. Certain writers (Sellors<sup>4</sup> and Overholt<sup>5</sup>) have included, as an indication, a stage, presumably with cavity already formed, which is too early to allow thoracoplasty owing to poor condition, toxemia, *etc.*, and lowered resistance. From an experience (Case 2) in which the operation, although performed under local anesthesia, was followed by a rapid spread in both lungs and death in eight weeks, we believe that extrapleural pneumothorax must be regarded as having a very definite risk in these cases. The rapid and extensive collapse which may follow doubtless breaks down local barriers to the spread of the disease, which may overcome resistance, local and general. We believe the inclusion of early cases, or of doubtful resisting powers, should be exceptional.

To the above list, possibly those cases should be added where repeated hemorrhages threaten to seriously reduce the patient but have not yet made operation too hazardous. While we have not treated any hemorrhage cases with extrapleural pneumothorax, it would seem to be indicated in certain cases.

*Contraindications.*—Since the possibility of successful production of the extrapleural air-pocket depends upon the absence of too firm adhesions between parietal pleura and chest wall, a very chronic condition with extensive or very dense lesions, especially with large cavities near the periphery, is a contraindication. There are three reasons for this:

- (1) There may be no line of cleavage in the endothoracic fascia, so that separation is practically impossible.
- (2) The danger of rupture of a thin-walled cavity, either during operation or later, is too great.
- (3) In thick-walled cavities it may be impossible to produce collapse even with positive pressure.

In these conditions, thoracoplasty is likely to be safer and more efficient.

Large cavities, unless centrally located and of not too great chronicity, are

also a contraindication, owing to danger of rupture. The occurrence of pulmonary fistula has been mentioned often enough in the published reports to prove that rupture of the cavity wall after operation is not rare (Overholt,<sup>5</sup> Sellors,<sup>4</sup> Pierre-Bourgeois and Lebel<sup>6</sup>). In the stripping-off of the fused pleural layers, the blood supply of a superficial cavity wall may well be destroyed. In long-standing disease, especially, it is probable that the chief blood supply of at least the peripheral aspect of the cavity is from small branches of the intercostal vessels which of course are ruptured in the stripping process. Therefore, we believe that a superficial cavity of more than 2.5 cm. is a contraindication, and that in such a case a thoracoplasty is far safer.

*Activity.*—As suggested in the discussion of *Indications*, active or too early lesions are a definite contraindication for reasons already stated.

*Technique.*—In the posterior approach, which we have used exclusively, the exposure of the extrapleural layer is made by an incision through the trapezius and rhomboid muscles, long enough to afford access to the fourth rib and allow subperiosteal removal of about four inches. The length and direction, whether vertical or oblique, will depend upon thickness of the muscles and, according to the surgeon's choice, whether the muscles are cut transversely or split between muscle bundles.

Coryllos<sup>2</sup> preferred resection of the third rib and the end of the corresponding transverse process, which exposes the third intercostal nerve lying on the endothoracic fascia and serves as a guide to the line of cleavage. Sellors<sup>4</sup> advises an oblique incision, division of two ribs near the spine without removal, spreading of the ribs after freeing the periosteum. He states that closure with a periosteal suture is easy to obtain.

We have employed an incision 2 to 3 cm. within the vertebral border of the scapula in the majority of our series.

The incision of the periosteal bed or intercostal muscle (Roberts<sup>7</sup>) must be made with great care in order not to injure the parietal pleura. The endothoracic fascia in most cases is a rather loose areolar layer of tissue, and the stripping is done *in this layer*, rather than between it and the parietal pleura (Coryllos), and the presence of fat is sometimes a guide to this layer (Overholt). Roberts advises incising the intercostal muscle rather than the periosteum to protect the underlying pleura from injury, but we believe this makes the final tight closure more difficult. The stripping is best begun by a wiping of the pleura with a gauze pledget held in a suitable clamp, but when once started the stripping of loose adhesions can be done with the finger, especially as the axillary region is approached. The apex should be freed as thoroughly as possible on all sides, and the stripping carried all around the diseased lung and to a level below the lesions in order to provide a "reserve of compression" (Schmidt). Overholt advises stripping to two rib spaces below the roentgenologic level of the cavity. This allows for possible readhesion at the lower margin of the air-pocket between refills. In order to control hemorrhage from torn vessels, an electric illumination of the cavity is indispensable, to render bleeding points visible. While smaller ones will close with brief pressure with

a gauze pack, larger ones may require clamping, or even inclusion in a silver clip or ligature.

Postoperative hemorrhage has been a serious complication in some reported cases and must be prevented by careful hemostasis before closure is begun. Overholt has devised flat ribbon retractors bearing an electric light at the end to facilitate this important step.

Extensive pleuritis may have produced dense bands which require cutting but this is unusual in our experience. Of course, occasionally an extreme degree of extrapleural fibrosis ("pachyexopleurite": Pierre, Bourgeois and Lebel) may render the stripping too difficult and the operation must be abandoned in favor of thoracoplasty.

The final closure of the periosteomuscular layer is accomplished by a continuous suture of fine catgut, which can be made easier by division of the periosteum of an adjacent rib and separating it sufficiently from the rib to relax the tissues at the suture line. Any possible gaps, through which air leakage may occur, should be reinforced by a muscle flap, for which the serratus superior often serves.

Before the patient is removed from the operating table, an injection of 50 to 100 cc. of air should be made, raising the manometer pressure reading to about + 5 cm.

*After-Treatment.*—Frequent refills should be carried out, especially during the first few days. As the air absorption may be rapid at first, refills every 12 hours for the first day or two may be necessary, the interval being gradually lengthened to every two days at the end of the week, and to once a week by the end of the month. If air is lost through emphysema, lower pressures and more frequent refills are necessary, but as healing of suture line and tissue spaces occurs, higher pressures are employed to maintain the collapse. Fluid, somewhat bloody at first, should be aspirated. Roentgenologic control of the air-pocket is of the greatest value. If this shows the floor of the pocket to be rising through readhesion at the margins, injection of sterile oil, as used by Schmidt, Brunner,<sup>8</sup> and others, should be resorted to. We have found this very useful. After the air-pocket becomes tightly sealed, pressures may be raised to + 15 or + 20 cm.

Higher pressures carry the danger of rupturing the cavity wall, which occurred in one of our cases. Escape of air through the suture line, forming an air-pocket under the muscles of the back, is another possibility.

*Duration of Treatment.*—As the situation after the establishment of an extrapleural pneumothorax (or oleothorax) is similar to an intrapleural pneumothorax, which requires two years or more for successful healing of the cavity, the treatment should be carried out at least as long. The operation is, therefore, too recent for any report on final results to be available.

*Complications.*—Postoperative hemorrhage into the air-pocket, perforation of the cavity wall, fistula, and resulting extrapleural empyema are the principal complications, any one of which may cause a fatality, or failure to maintain

collapse, which will demand a subsequent thoracoplasty. This occurred seven times in Schmidt's series of 155 cases.

*Results.*—The largest series of cases as yet reported is that of Schmidt. In 155 cases, there were two operative deaths following extrapleural pneumothorax, an operative mortality of 1.2 per cent. There were nine deaths later, a total mortality of 7 per cent; 52 cases required oleothorax; 124 showed a satisfactory collapse.

*Experiences and Results with 32 Cases at the Boston Sanatorium.*—During the past 14 months, extrapleural pneumothorax has been attempted or carried out in 33 cases, in one of which firm adhesions prevented stripping of the pleurae from the chest wall, and thoracoplasty was performed. Of the 32 cases in which the extrapleural operation was performed, all were cases of more or less advanced disease of a duration varying from ten months to 16 years. Thirty cases were of unilateral, and two of bilateral, apical disease. All were performed under local anesthesia (novocain) preceded by morphine and scopolamine, and supplemented by gas-oxygen inhalation, during the process of stripping the pleura, in most cases. In only one case was there a severe degree of shock; in all others this was slight or moderate. Two cases died, one (J. D., Case 1) on the twelfth day; the second (J. R., Case 2), after two months, the latter having bilateral disease.

In the first two cases operated upon, the stripping was not carried far enough and the resulting air-pocket was insufficient to produce effective collapse and, while the cough and expectoration were greatly diminished, the sputum remained positive. One of these has had a secondary operation after ten months of refills. This operation was carried out without difficulty and a large air-pocket established. In the other case, the patient has so far refused a second operation.

In the third case to be operated upon, a small air-pocket was quickly lost through air leakage and adhesions reforming, and a thoracoplasty was performed four months later. Although a second stage has been recently carried out, the sputum is still positive.

Seven cases have been discharged from the hospital in good physical condition and with negative sputa, and are returning every week or two for refills.

In several of the earlier cases, air was injected under excessive pressure, which in two cases resulted in escape of air under the back muscles, rendering the collapse less effective, and in a third case a pulmonary fistula developed, causing infection of the air-pocket, which is now being kept open by a drain and irrigated. The sputum remains positive. The final result is uncertain as the collapse is insufficient (Fig. 1 and 2).

Collections of fluid, at first bloody, later becoming serous, occurred in 15 cases (47 per cent) and of these, eight were treated by aspiration when refills were undertaken. In two, the fluid became purulent, and gomenol has been injected, apparently with good effect. One purulent case has developed a spread to the other lung.



# EXTRAPLEURAL PNEUMOTHORAX

(Before)

(After)

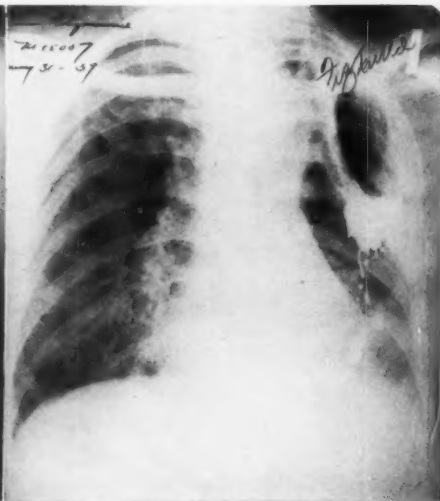
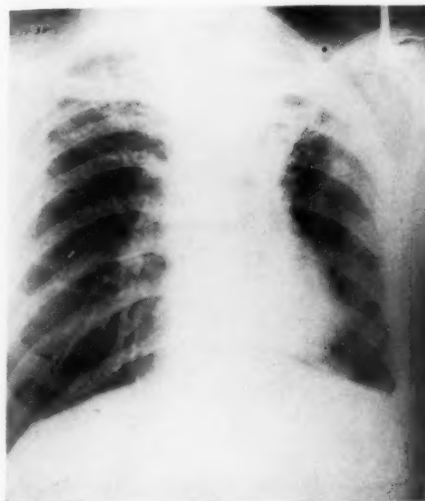


FIG. 1

FIG. 2

FIGS. 1 and 2.—Medium-sized cavity, left upper lobe. Disease of three years' duration. Small air-pocket obtained. High pressures used, probably excessive, as fistula developed through cavity wall. Drainage sinus developed in operation wound. Picture shows lipiodol in bottom of air-pocket, below level of fistula.

(Monaco)

(Johnson)

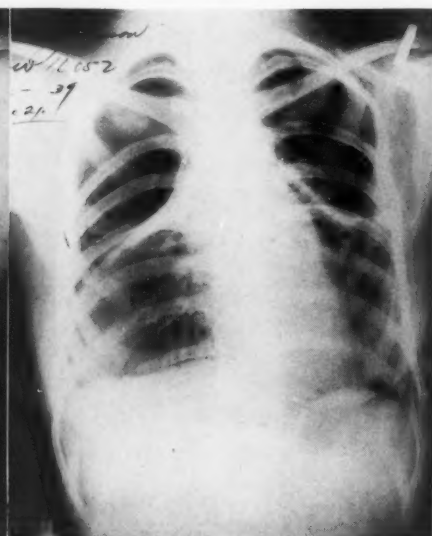


FIG. 3

FIG. 4

FIG. 3.—Illustrating case in which good collapse obtained with large air-pocket, and sterile effusion (serous).

FIG. 4.—Illustrating bilateral disease, operated upon in two stages. Complete relief of symptoms and conversion of sputum.

In 27 cases of the 32, a satisfactory air-pocket was obtained, and in 20 (62 per cent) a conversion of sputum effected.

#### Summary of results

Operation impossible, requiring thoracoplasty:.....	1 case
Extrapleural pneumothorax carried out.....	32 cases
Fluid (sterile) developed.....	15 cases (47.0%)
Fluid (purulent) developed.....	2 cases ( 6.2%)
Satisfactory collapse obtained.....	27 cases (84.3%)
Collapse unsatisfactory, requiring later operation (thoracoplasty)...	3 cases ( 9.2%)
Conversion of sputum.....	20 cases (62.0%)
Cases made outpatients.....	7 cases (21.8%)
Deaths.....	2 cases ( 6.2%)

#### ANALYSIS OF FATALITIES

**Case 1.**—J. D., female, age 32, single, was admitted, April 12, 1938, with a history of phthisis of 11 years' duration. Treated at other sanatoria from 1927 to 1931, during which time a right phrenicectomy was performed; then at home until admission. Examination

(D'Amato)

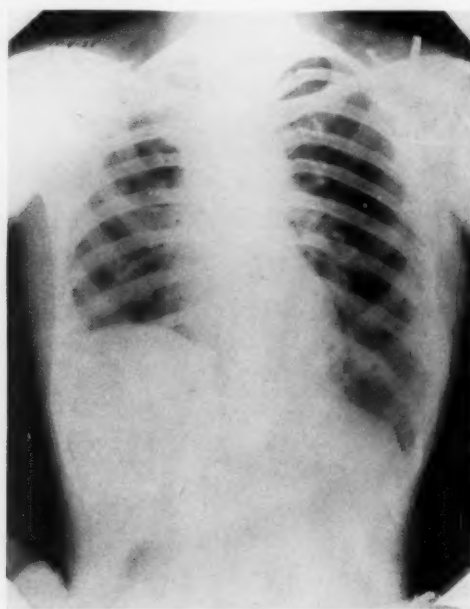


FIG. 5.—Case 1: Large cavity in right upper lobe. At operation, good collapse obtained and 150 cc. air injected into extrapleural pocket. After third day, increasing dyspnea, due to rupture of cavity wall; partially relieved by daily removal of air. Death on twelfth day.

showed normal temperature, respirations 20 to 24, slight cyanosis, signs of involvement of right apex, right diaphragm high. Sputum positive, two ounces in 24 hours. Attempts at pneumothorax unsuccessful. During next six months, large cavity developed in right upper lobe. Left lung showed few râles at apex but negative roentgenologically. General condition fair. Vital capacity = 1,000 cc. (Fig. 5.)

Owing to failure to improve, and increase in size of cavity, extrapleural pneumothorax

## EXTRAPLEURAL PNEUMOTHORAX

decided upon, and performed under local anesthesia, October 28, 1938. During operation, patient showed marked shock, but with stimulation and intravenous glucose, operation completed, and 150 cc. of air injected into air-pocket. Patient placed in oxygen tent. Condition improved during next three days under continuous oxygen. On fourth day, increased dyspnea present. Pressure in air-pocket found positive and 75 cc. air removed. Relief only temporary. Fluid and air removed daily but pressure continued positive, evidently due to a rupture of the cavity wall. Patient gradually failed, and died on 13th day, with signs of bronchopneumonia in left lung. No autopsy.

In this case, the low vital capacity and large cavity near the periphery of the lung should have warned us against even extrapleural pneumothorax.

**Case 2.**—J. B., male, Negro, age 22, married, was admitted, March 29, 1938, with history of three months' cough and loss of weight. Sputum found positive one week pre-

(Before)

(Robinson)

(After)

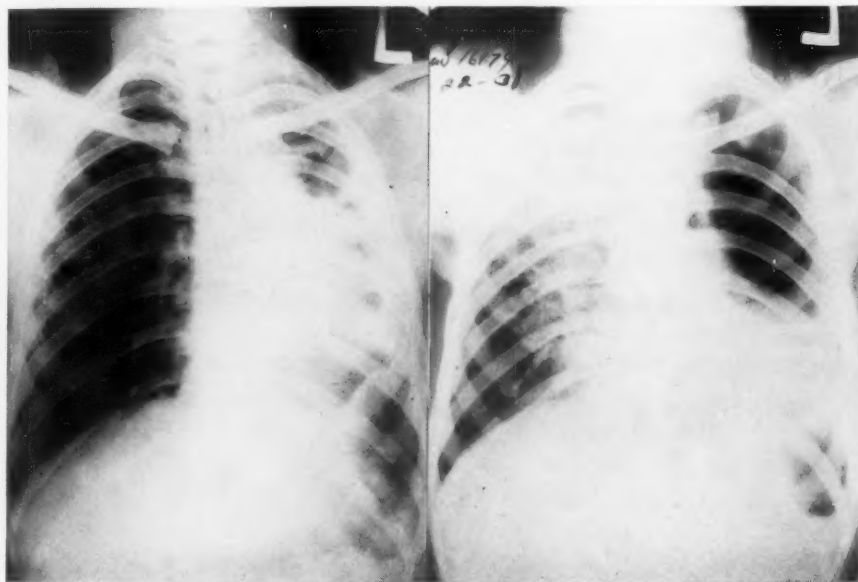


FIG. 6

FIG. 7

FIGS. 6 and 7.—Case 2: Multiple cavities left upper lobe. Operation produced good collapse and large air-pocket. In third week, signs in right lung. Increase of cough and sputum, finally hemorrhage and death on sixty-fourth day.

viously. Examination showed a pale, poorly nourished patient with diffuse involvement of both lungs, especially marked in left upper lobe. Put on bed rest for three months. After several unsuccessful attempts at pneumothorax, a left phrenic paralysis performed. During next three months, ran a moderate temperature. Condition in right lung improved, left remaining unchanged. Roentgenograms showed density of left upper lobe, clinical signs of cavity present. Extrapleural pneumothorax advised, and performed, October 21, 1938. Good collapse obtained but cough soon increased, temperature more elevated, and signs of spread to right lung appeared. After a month, a severe hemorrhage occurred and right intrapleural pneumothorax given without success in control of streaking. Patient failed and died four days later, 64 days after operation. Autopsy showed extensive fibrocavernous disease in both lungs, more marked on the left side (Figs. 6 and 7).

This patient evidently had not developed sufficient resistance to stand the rapid and extensive collapse of the more diseased lung. The prognosis in a

Negro being poor under any conditions, the attempt to prevent further extension of the disease by surgery was an error in judgment.

## CONCLUSIONS

Extrapleural pneumothorax has the advantage of being suitable for local anesthesia, of having less shock, and a lower rate of mortality than thoracoplasty. It cannot, however, be safely applied in early cases with low resistance, nor is it suitable in large cavities or in those over 2.5 cm. in diameter, when very superficial, nor in long-standing cases with dense lesions. Here the pleurae are likely to be too adherent to the chest wall, and thoracoplasty is necessary. While rapid in symptomatic benefit, and often in conversion of sputum, the after-treatment with refills must be prolonged—how long we are not yet in a position to judge.

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## BOWEL OBSTRUCTION IN THE NEW BORN\*

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THE INFANT presenting evidence of bowel obstruction immediately after birth or within the first few days of life deserves the best attention of the pediatrician and the surgeon. Fortunately, these cases do not occur often, but perhaps this relative infrequency of occurrence itself may cause the physician who first sees the baby to overlook the likelihood of a real obstruction, and, therefore, to delay surgical interference too long. I feel sure that this may be accountable for some unnecessary deaths.

The frequency of occurrence of a congenital obstruction in the new born, excepting of course the not uncommon imperforate anus, is difficult to estimate accurately. No report of this kind appeared in the literature until that of Calder<sup>1</sup> of Edinburgh, in 1733. Theremin,<sup>2</sup> in 1877, found only nine cases in 150,000 autopsies in the Foundling's Hospital in St. Petersburg. Tandler<sup>3</sup> of Vienna, in 1900, collected 94 reports, and Davis and Poynter<sup>4</sup> of Omaha, in 1922, had gathered a total of 392. Up to the present time, well over 500 cases have been recorded, and most authors seem to feel that perhaps 1 in 20,000 infants at birth are thus affected.

Many different theories have been advanced to explain the wide variety of pathologic conditions that may produce a partial or complete congenital obstruction, yet the probabilities are that the great majority of them can easily be interpreted on the basis of errors or defects in embryologic development. The very fact that most of them are located in the duodenum near the ampulla of Vater, and the terminal ileum close to Meckel's diverticulum, strongly supports the contention that these anomalies occur at the sites of the most complex embryologic changes, an opinion first stated by Bland-Sutton<sup>5</sup> in 1889.

The pathology is well understood. The literature concerned with congenital bowel obstruction up to within the last 25 years was almost a continuous, uninterrupted series of autopsy reports and citations of fatal cases, as it was not until 1911 that the first successful operation for atresia of the ileum was performed by Fockens<sup>6</sup> of Rotterdam, and not until 1916 that Ernst<sup>7</sup> of Copenhagen published the first successful operation for atresia of the duodenum. These two papers still stand as milestones in the field of intestinal surgery in infants. In general, two main types of pathology are recognized: (1) The intrinsic, consisting usually of a complete gap or interruption in the continuity of the bowel; sometimes a cord-like remnant of the lumen insufficient in caliber to permit the passage of intestinal content; and, more rarely,

\* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.



a septum or iris-like diaphragm acting as a partition to block the channel (Seidlin,<sup>8</sup> and Garvin<sup>9</sup>). (2) The extrinsic, caused by abnormal folds of peritoneum, adhesions left by fetal peritonitis, direct pressure from overlying large vessels (*i.e.*, the root of the mesentery across the third portion of the duodenum), or a faulty rotation of the cecum or ascending colon, leading to a volvulus of the midgut on the axis of the superior mesenteric artery and abnormal fixation of the cecum in a position where it partially or completely blocks the duodenum close to its junction with the jejunum. Davis and Poynter,<sup>4</sup> in their analysis of 392 recorded cases up to 1922, showed that 134 occurred in the duodenum (59 above the ampulla, and 75 below it), 60 were in the jejunum, 101 were found near or at the terminal ileum, and only 39 in the colon. In 76 instances the lesions were multiple.

Early recognition of an obstruction in the new born is essential if successful results are to be expected and the high mortality materially reduced. The physician first to see the infant must, therefore, be alert to the possibility of its presence. In the differential diagnosis of every case of pylorospasm or congenital pyloric stenosis, especially in the absence of a palpable tumor, and particularly if the vomiting begins early (after the first nursing or within the first few days of life), one must always consider the possibility of a partial or complete obstruction in the first portion of the duodenum. The presence of bile in the vomitus gives one a valuable clue, and the clinical picture of persistent biliary vomiting coupled with visible peristaltic waves in the epigastrium, a flat lower abdomen, and rapid dehydration is almost unmistakable evidence of an obstruction of the duodenum below the ampulla of Vater, in all probability due to a true atresia, pressure from the overlying superior mesenteric vessels, or a twist at the duodenojejunal junction. A persistent vomiting which soon becomes fetid in odor and brown in color, and is associated with general abdominal distention and obstipation can mean only one thing, *i.e.*, a partial or complete obstruction lower down, probably in the terminal ileum. In any case where a doubt exists, it is a wise plan to verify one's suspicion roentgenologically, by giving a little thin barium mixture by mouth if the obstruction seems to be high, or by giving barium as an enema if the obstruction seems to be low. In the former, the exact lower limit of the obstruction can thus be easily demonstrated, and in the latter, the visualization of the collapsed colon will help to confirm one's impression of the lesion being proximate to the ileocecal valve.

What chance, you may ask, has a new born baby thus afflicted, with a complete or almost complete obstruction in the duodenum or small bowel, to survive beyond a period of a few days or at most a few weeks? I can best answer that question by referring to the evidence from the literature and adding to that evidence certain impressions which I have gained from my own experience.

Group A. If the obstruction is in the *jejunum* or *ileum*, the chances of recovery are very small, because, during a period of over 100 years, there have been only three successful results reported.

## BOWEL OBSTRUCTION IN NEW BORN

**Case 1.**—Fockens, P.,<sup>6</sup> Rotterdam, 1911: Vomiting since birth becoming fecal in character. On seventh day after birth brought to hospital. Abdomen distended and tympanitic. Visible peristalsis. At operation on eighth day, a gap in lower ileum 4 cm. long bridged by fibrous cord. *Lateral anastomosis*. Recovery.

**Case 2.**—Demmer, Fritz,<sup>10</sup> Vienna, 1921: On September 22, 1921, new born infant brought to hospital, presenting evidence of a tumor in region of navel and complete obstruction of small bowel. At operation an atresia of terminal ileum with 14 cm. gap. Resection of vestige of cecum. *Lateral anastomosis*. Recovery.

**Case 3.**—Carter, R. F.,<sup>11</sup> New York, 1933: Infant four days old. No bowel movement since birth. Fecal vomiting for 12 hours. Moderate distention and visible peristalsis. At operation an atresia of lower ileum with cord-like structure attaching it to the cecum. Proximal bowel greatly dilated, distal collapsed. *Lateral anastomosis* between ileum and descending colon. *Ileostomy* proximal to anastomosis. Recovery.

**COMMENT.**—Anyone who has had experience with this type of case will be able to appreciate the reasons for the high mortality in this group. The baby is usually in poor condition when it comes to operation; the proximal bowel is not only greatly dilated but often beginning to show signs of necrosis. The distal bowel has never functioned and is collapsed—usually the size of a small lead pencil. Even if a lateral anastomosis can be made, the thick, viscid meconium in the distended bowel cannot readily pass on into the distal segment. There has never been a successful result recorded where ileostomy alone has been used.

**Group B.** If the obstruction is in the *duodenum* and produces a complete or almost complete block of the lumen, which requires some sort of short circuiting anastomosis, the outlook, while still bad, is considerably brighter than in Group A. Moreover, the prospects for still better results are very encouraging. In this group successful operative results are limited to the following 16 cases:

**Case 1.**—Ernest, N. P.,<sup>7</sup> Copenhagen, 1916: Male infant. Vomiting began with first feeding and continued. Rapid loss of weight. Dehydration. Operation on eleventh day showed duodenum greatly dilated down to upper margin of transverse colon. Jejunum collapsed. *Duodenojejunostomy* (antecolic). Recovery.

**Case 2.**—Weeks, A., and Delprat, G. B.,<sup>12</sup> 1916: Infant six days old. Congenital atresia of third portion of duodenum. Stomach and duodenum presented gross appearance of hourglass stomach. *Gastro-enterostomy*. Recovery.

**Case 3.**—Higgins, T. T.,<sup>13</sup> London, 1923: Male infant one week old. Biliary vomiting since birth. No bowel movement after second day. Emaciation. Visible gastric peristalsis. Roentgenograms after giving barium showed obstruction of lower duodenum with few flecks passing after 45 minutes. Mass in region of pancreas. Jejunum collapsed. *Posterior gastro-enterostomy*. Recovery.

**Case 4.**—Richter, H. M.,<sup>14</sup> Chicago, 1924: Infant four days old. Atresia of duodenum. *Posterior gastro-enterostomy*. Recovery.

**Case 5.**—Cutler, G. D.,<sup>15</sup> 1924, cited by Clara Loitman: Infant four days old. Congenital obstruction of duodenum. *Posterior gastro-enterostomy*. Recovery.

**Case 6.**—Steward, M.,<sup>16</sup> London, cited by H. C. Cameron, 1925: Female infant. On third day began vomiting bile. Seen on fifth day. Meconium stool. Distention of the abdomen. Roentgenograms showed duodenum greatly distended with barium. Few flecks passed into jejunum. *Posterior gastro-enterostomy*. Recovery.

**Case 7.**—Bowling, R. W.,<sup>17</sup> New York, 1926: Female infant. Vomiting began with first nursing and continued. Meconium stools. Roentgenograms showed complete ob-

struction and great dilatation of the duodenum. Operation on ninth day. Weight 5 lbs. *Duodenojejunosotomy* (antecolic). Recovery.

**Case 8.**—Sweet, G. B., and Robertson, C.,<sup>18</sup> New Zealand, 1927: Female infant nine days old. Vomiting began with lactation and persisted, becoming projectile. Very little meconium. Loss of weight. Visible gastric peristalsis. Operation on tenth day. Duodenum dilated in third portion. Jejunum collapsed. *Anterior gastro-enterostomy*. Home on ninth day. Twelve days later, returned to hospital with vomiting as before. *Duodenojejunosotomy* performed. Recovery.

**Case 9.**—Porter and Carter,<sup>19</sup> cited by Clara Loitman, 1927: Infant successfully operated upon for congenital atresia of the duodenum. After four years, in perfect health. Type of operation not stated.

**Case 10.**—Ladd, W. E.,<sup>20</sup> Boston, 1932. Hosp. No. A5528: Premature infant, four days old. Vomiting since birth. Visible epigastric peristalsis. Complete retention of barium in duodenum after four hours. *Posterior gastro-enterostomy*. Recovery.

**Case 11.**—Ladd, W. E.,<sup>20</sup> Boston, 1932. Hosp. No. 3599: Female infant, age six days. Vomiting since birth. Intrinsic obstruction of duodenum. *Posterior gastro-enterostomy*. Recovery.

**Case 12.**—Donovan, E. J.,<sup>21</sup> New York, 1936: Cesarean baby. Biliary vomiting since birth. Roentgenogram on ninth day showed obstruction at third portion of duodenum. At operation obstruction seemed to be due to pressure by superior mesenteric vessels. *Duodenojejunosotomy* (antecolic). Three rows of suture. Recovery.

**Case 13.**—Donovan, E. J.,<sup>21</sup> New York, 1936: Male infant. Seen at age of 17 days. Biliary vomiting since birth. Upper abdomen distended. Visible epigastric peristalsis. Roentgenograms show duodenum greatly dilated with small particles of barium passing after 40 minutes. Duodenum as large and thick-walled as the stomach. Obstruction seemed under superior mesenteric vessels. *Duodenojejunosotomy* (antecolic). Three rows of suture. Recovery.

**Case 14.**—Morton, J. J., and Jones, T. B.,<sup>22</sup> Rochester, N. Y., 1936: Infant four days old. Vomiting began 48 hours after birth. Dehydration. Visible gastric peristalsis. Mongolian idiot. *Posterior gastro-enterostomy*. Duodenum greatly dilated and walls very thin. Recovery. Two years later death from pneumonia. Autopsy showed congenital absence of third portion of duodenum.

**Case 15.**—Morton, J. J. and Jones, T. B.,<sup>22</sup> Rochester, N. Y., 1936: Female infant. Vomiting began fifth day. On twelfth day, visible gastric peristalsis. Roentgenograms with barium showed complete block in second part of duodenum. At operation the dilated duodenum was opened longitudinally at point of obstruction and a 2 Mm.-thick diaphragm removed with electric cautery. Bowel closed transversely. Convalescence stormy. Recovery.

**Case 16.**—Tallerman, K. H., and Levi, D.,<sup>23</sup> England, 1938: Male infant, age 15 weeks. Began vomiting biliary material one day after birth. On sixth day roentgenogram showed obstruction in second part of duodenum. At operation an *anterior gastro-enterostomy*. On third day, wound was opened and a gastrostomy performed because of failure of anastomosis to function. On seventeenth day, abdominal wound resutured. Bile continued to leak and digest the skin. Recovery after two months.

COMMENT.—It will be seen that up to 1918, only two cases in this group had been successful. By 1928 (ten-year period), only seven had been added, and at the end of 1938, there was a total of 16. It will be noted also that in these 16 successful operations a gastro-enterostomy was performed nine times, a duodenojejunosotomy five times, the duodenum was opened and a septum removed once (Morton and Jones) and in one case the type of operation was not stated. I am of the opinion that in the high obstructions of the duodenum (above the ampulla of Vater) a gastro-enterostomy is the procedure of

choice. In the lower obstructions, in which the degree of dilatation of the duodenum is great, a duodenojejunosomy is preferable. Naturally, the technic is difficult, because one is making an opening between a dilated viscus and a jejunum which has never functioned and has the caliber of a goose-quill. Under these conditions, injection of air or water into the collapsed jejunum, as advocated by Webb and Wangenstein,<sup>28</sup> may facilitate the procedure, and the employment of only two rows of suture makes it technically easier. It is obvious, of course, that the employment of the finest needles and silk is essential to success.

Group C. In addition to the 19 successful cases in Groups A and B, there have been six others in which the obstruction was due to an abnormal band or an adhesion, and by the removal or severance of this structure the continuity of the bowel was successfully reestablished. Five of these involved the duodenum and one the ileum.

**Case 1.**—Jewesbury, R. C., and Page, Max,<sup>24</sup> England, 1922: Female infant. Vomiting of bile since first feeding. Loss of weight. Roentgenogram showed obstruction between second and third portion of duodenum. At operation (Mr. Page) on twelfth day, the first part of jejunum was found to be twisted and fixed by adhesions which were divided. Recovery.

**Case 2.**—Jackson, Reginald,<sup>25</sup> Madison, Wis., 1926: Female infant, seven days old. Projectile vomiting began third day. Weight 4½ lbs. Barium given and partial obstruction seen in region of pylorus. Next few days, vomitus contained bile. At operation, on twenty-first day, a dense vascular veil was found compressing second portion of duodenum. This was divided. Recovery.

**Case 3.**—Carter, R. F.,<sup>11</sup> New York, 1933: Infant seven days old. Vomiting since birth, projectile in character. No abdominal distention. Roentgenogram with barium showed complete occlusion of first part of duodenum. At operation a fibrous band was divided and the obstruction relieved. Recovery.

**Case 4.**—Davenport, G. L., and Goldberg, S. L.,<sup>26</sup> Chicago, 1934: Premature infant. Vomiting, distention, absence of stools. At operation, on third day of life, loops of upper jejunum distended. Obstruction caused by adhesion to parietal peritoneum in left upper quadrant. Released. Recovery.

**Case 5.**—Morton, J. J., and Jones, T. B.,<sup>22</sup> Rochester, N. Y., 1936: Infant few days old. Roentgenogram showed obstruction in duodenum. At operation duodenum was fixed by adhesions in several places. These were divided. Recovery.

**Case 6.**—Stenson, Walter,<sup>27</sup> New York, 1938: Female infant, four days old (eight months premature twin). Vomiting began fourth day. Barium roentgenogram showed obstruction in second part of duodenum. At operation a band was divided in front of duodenum. Portal vein accidentally opened. Bleeding controlled by packing. Convalescence stormy. Recovery.

To this list, I wish to add my own experience with 14 cases of congenital obstruction covering a period of the past 13 years, six involving the jejunum and ileum with a fatal result in each case, and eight involving the duodenum, four of which resulted successfully.

#### CASE REPORTS

##### JEJUNUM AND ILEUM

**Case 1.**—Infant Carey. Born at Presbyterian Hospital, December 5, 1925, with abdomen greatly distended. Few large peristaltic waves seen about umbilicus. Barium

enema roentgenogram showed collapsed colon. On December 6, 1925, a plain roentgenogram showed great distention of loops of ileum. Operation under local anesthesia. McBurney incision. *Ileostomy*. On January 16, 1926, the ileostomy was closed, with resection and lateral anastomosis. January 22, 1926, death from peritonitis. *Autopsy*: Terminal three inches of ileum size of goose-quill.

**Case 2.**—Infant Susie Brown (Fig. 1), age two days. Cook County Hospital.

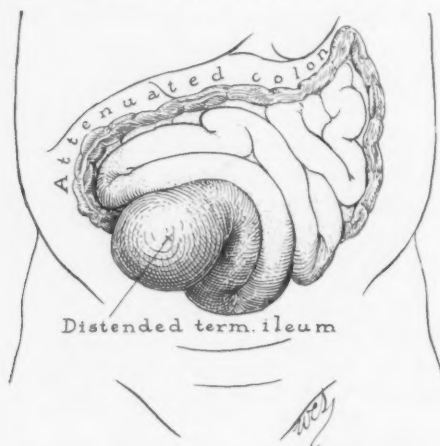


FIG. 1.—Case 2: Age two days. Congenital obstruction at the terminal ileum. *Ileostomy*. Death.

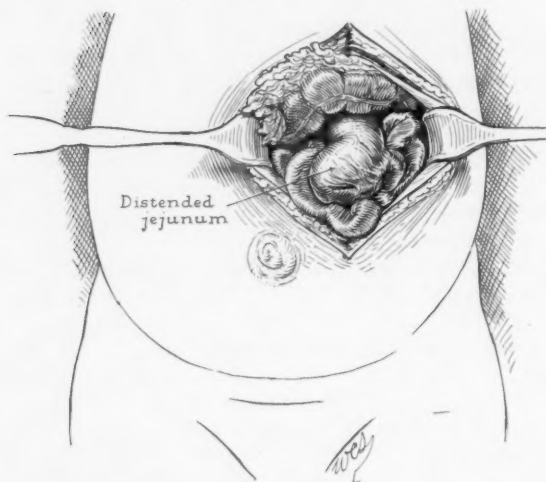


FIG. 2.—Case 3: Age two days. Congenital obstruction of the jejunum from adhesions. Adhesions divided. Death from pneumonia, four days after operation.

Vomiting since birth. Distention progressively more marked, involving entire abdomen. *Operation*.—July 10, 1929: Entire small bowel distended, most marked at cecum. Entire colon collapsed, rudimentary in size—average diameter about 1 cm. *Ileostomy*. Content of terminal ileum thick, tenacious meconium which could not drain. Death in 24 hours.

**Case 3.**—Infant May Jones (Fig. 2), age two days. Cook County Hospital. Vomiting since birth. No bowel movement except meconium. Distention of upper abdomen



## BOWEL OBSTRUCTION IN NEW BORN

becoming progressively worse. *Operation*.—October 2, 1929: Obstruction in upper jejunum from adhesions between two loops of bowel. Above distention, below collapse. Adhesions divided, allowing distal loop to fill at once. October 6, 1929, death from pneumonia.

**Case 4.**—Infant Heag (Fig. 3), age three days. Cook County Hospital. Admitted January 10, 1931. Vomiting bile stained material ever since birth. Marked distention of entire abdomen. *Operation*.—January 10, 1931: Ether. Evidence of general peritonitis. Loops of ileum greatly dilated down to point where there is complete obstruction, beyond which ileum is collapsed. Six inches of bowel proximal to obstruction is black and gangrenous. *Lateral anastomosis*, but case considered hopeless. Death in 24 hours.

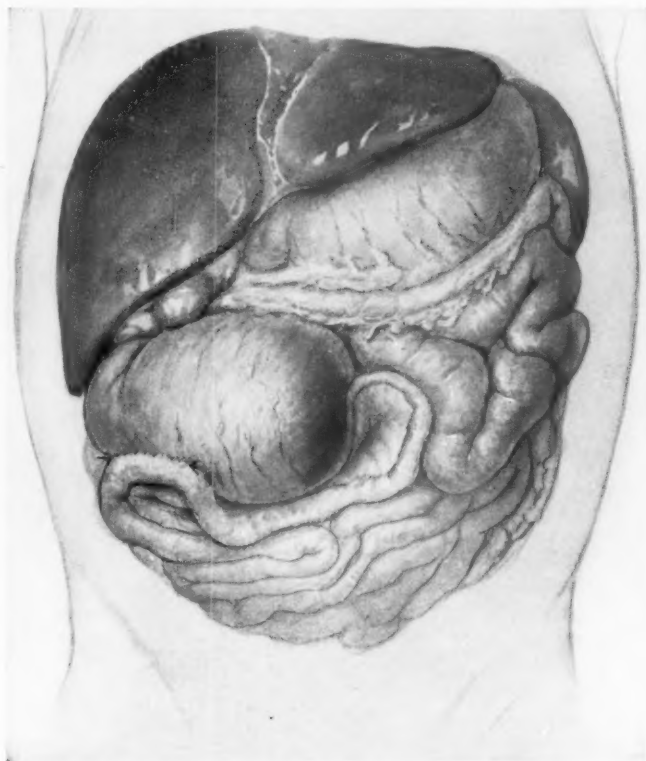


FIG. 3.—Case 4: Age three days. Congenital atresia of the upper ileum. Lateral anastomosis. Death 24 hours after operation.

**Case 5.**—Infant Wisnewski (Fig. 4), age one week. Born at Cook County Hospital, June 8, 1931, with apparent congenital bowel obstruction. Seen by Doctor Parmelee who found narrowing of rectum two inches above orifice, which was considered cause of the obstruction. *Operation*.—June 10, 1931: *Sigmoidostomy*. Colon empty. Vomiting continued. Soon apparent that obstruction must be higher. *Second Operation*.—June 15, 1931: Small bowel obstruction about 15 ins. above ileocecal valve. Above this great dilatation, below bowel collapsed. *Lateral anastomosis*. Death June 16, 1931. No autopsy.

**Case 6.**—Infant Peter DeFrancisco (Fig. 5), age six days. Born January 15, 1935 at Cook County Hospital. Weight 5 lbs., 12 oz. Vomiting since birth. Nothing per rectum. Great distention of abdomen and tympany. Dehydration. Enema and blocked tube three inches up. Loss of weight. *Operation*.—January 21, 1935: Complete obstruc-

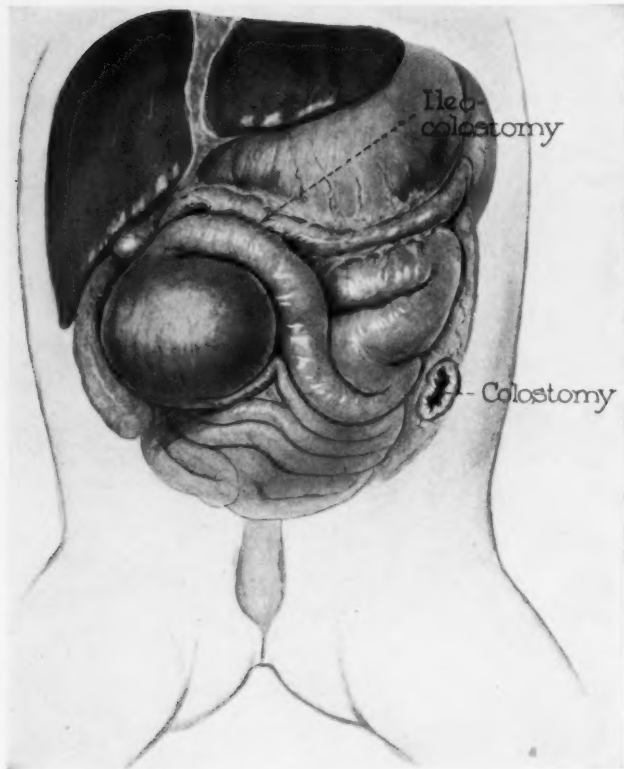


FIG. 4.—Case 5: Age one week. Congenital atresia of the upper ileum plus an imperforate anus. Lateral anastomosis after sigmoidostomy. Death.



FIG. 5.—Case 6: Age six days. Congenital obstruction of the midileum. Lateral anastomosis. Death from pneumonia 24 hours after operation.

# BOWEL OBSTRUCTION IN NEW BORN

tion of midportion of ileum. Bowel above 6 cm. wide, below 6 Mm. wide. Deflation with needle. *Lateral anastomosis.* Death January 22, 1935. *Autopsy:* Atresia at junction and middle one-third. Bronchopneumonia.

## DUODENUM

**Case 7.**—Chiuso, Rose (Fig. 6), Mongolian, age three weeks. Birth at Presbyterian Hospital. Weight 7 lbs., 2 oz. Admitted to Presbyterian August 18, 1930. Two days after infant was brought home from hospital, she began vomiting projectily after every

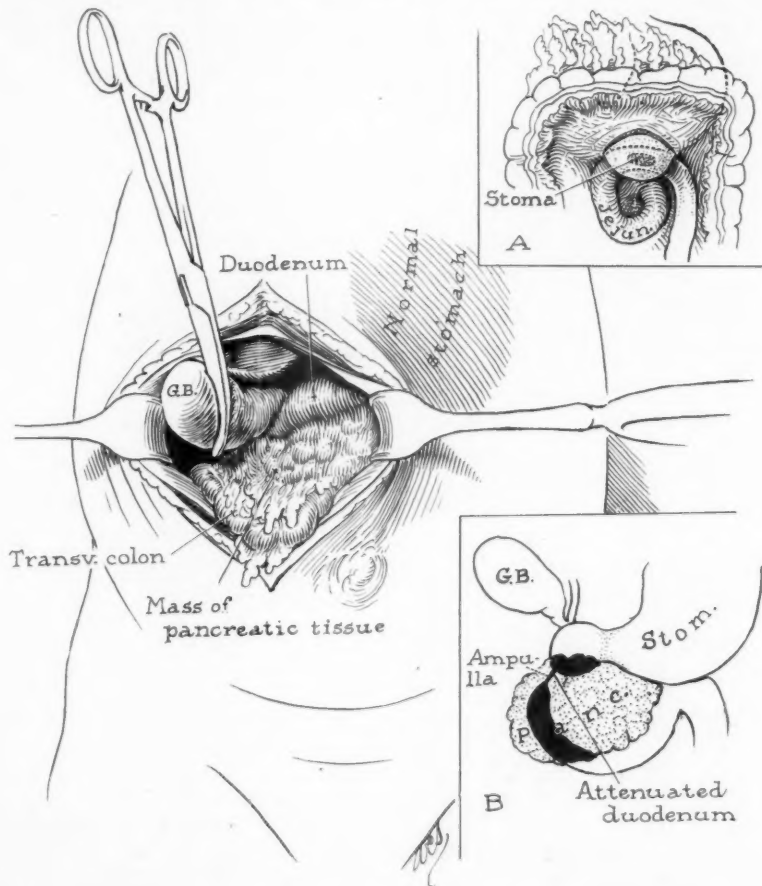


FIG. 6.—Case 7: Age three weeks. Congenital atresia of the duodenum. Posterior gastro-enterostomy. Recovery. Death from pneumonia five weeks later.

feeding. Dehydration. Visible epigastric peristalsis. Small tumor mass palpable in right upper quadrant. Pustule in right inguinal region. Vomitus bile stained. Peristaltic waves. *Operation.*—August 20, 1930: Local anesthesia. Rectus incision. No pyloric tumor. Beyond first 2½ inches of duodenum it could not be followed. Merely pancreas in view. Below pancreas duodenum again seen as far as upper margin of transverse colon. *Posterior gastro-enterostomy* performed because of evident atresia in region of ampulla of Vater. Three-row method with one clamp on both stomach and jejunum. Postoperative course uneventful. Recovery. One month later, developed pneumonia and died September 24, 1930. *Autopsy:* Gastro-enterostomy patent with no leak. An atresia of the duodenum 14 Mm. long, in center of which the ampulla of Vater opened.

**Case 8.**—Ross, Marion (Fig. 7). Born February 25, 1931. Weight 8½ lbs. Soon after birth, began projectile vomiting and did not take food well. Roentgenograms at first showed no opening at pylorus, but later, a little barium passed into small bowel. Diagnosis made of congenital pyloric stenosis, after failure to obtain relief of vomiting by atropine or luminal. Diagnosis confirmed by Doctor Grulee, who thought he could feel a pyloric tumor. Once or twice, a small amount of bile was noticed in the material vomited. *First Operation.*—March 11, 1931: Infant was 16 days old. Weight 6½ lbs. Right rectus incision under local anesthesia. Pylorus normal. First two inches of duodenum wider than normal and could not be followed further. Abdomen closed. Vomiting continued. *Second Operation.*—March 13, 1931: Under ether anesthesia. Left paramedian incision. *Posterior gastro-enterostomy.* Postoperative course uneventful after first few days. Recovery.



FIG. 7.—Case 8: Age nine. Congenital atresia of the second portion of the duodenum. Posterior gastro-enterostomy performed at age of two weeks. Excellent health eight years later.

**Case 9.**—Olson, Richard, age four days. Admitted to Presbyterian Hospital June 28, 1931. Infant born at home three days previously, apparently normal. Mongolian type. Biliary vomiting for past three days. Visible peristalsis. Condition poor. *Operation.*—June 29, 1931: Stomach and duodenum distended with gas. Jejunum collapsed. *Posterior gastro-enterostomy.* No clamp used. Diagnosis congenital atresia of third portion of duodenum probably just below ampulla of Vater. Death on following day. No autopsy.

**Case 10.**—Wilder, Frank (Fig. 8), age seven years. July 26, 1931, admitted to Cook County Hospital. Abdominal

pain. Inability to pass gas per rectum for 38 hours. Vomiting for two hours. When he was a baby had a Ramstedt operation for congenital pyloric stenosis. Since then he has had many attacks of what appeared to be partial intestinal obstruction, each lasting from two days to three weeks. Present attack began 38 hours ago with pain over entire abdomen, localized chiefly in umbilical region, associated with vomiting and inability to pass gas. July 27, 1931, discharged from hospital much relieved.

November 5, 1931, readmitted to hospital, complaining of cramp-like, intense pain for 13 hours. Vomiting for eight hours. Examination. General tenderness, distention. November 6, 1931, vomiting persisting. *Operation.*—Right rectus incision. There had been complete failure of rotation of intestine so that all of small bowel lay in front of colon. No retroperitoneal duodenum. Volvulus of midgut on axis of superior mesentery artery causing obstruction at duodenojejunal junction. Bowel had become more or less fixed in this position by adhesions. Veins greatly distended. Lymph nodes enlarged. Cecum lay near midline above umbilicus. Adhesions divided, permitting rotation of bowel back to normal position. December 22, 1931, discharged. Follow-Up: Seen in Clinic June 28, 1932, January 28, 1938, and January 10, 1939; appeared to be in perfect health since operation (Fig. 9).

**Case 11.**—Schmidt, Phyllis (Fig. 10), age five months. Born June 20, 1935. Weight 5 lbs. Cook County Hospital. November 20, 1935, admitted to hospital. Weight 12 lbs., 11 oz. History of vomiting more or less since birth. Nose, lips, hands and feet always blue.

Examination: (1) Congenital heart. (2) Vomiting of bloody material. Stools posi-

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FIG. 8.—Case 10: Age seven. Complete obstruction at the duodenojejunal angle following repeated attacks of partial obstruction since infancy. Pathology: Volvulus of midgut and incomplete rotation of the colon. Operation: Adhesions freed and volvulus untwisted. Recovery. Excellent health seven years later.



FIG. 9.—Case 10: Operated upon in 1931, seven years ago, for chronic obstruction at the junction of the duodenum and jejunum, due to rotation of the small bowel on the axis of the superior mesenteric artery.

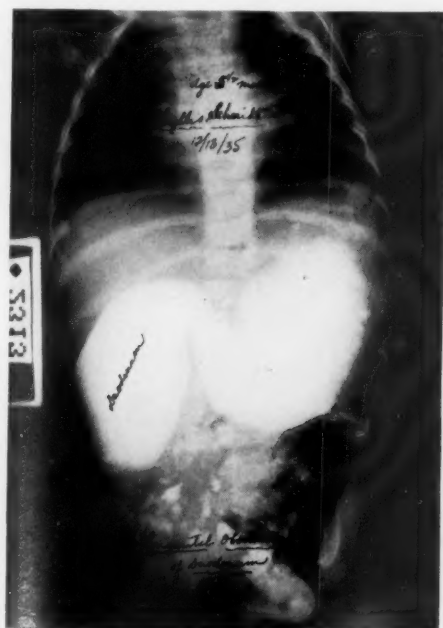


FIG. 10.—Case 11: Age five months. Congenital, partial obstruction of the duodenum. Duodenojejunostomy. Death from pneumonia.

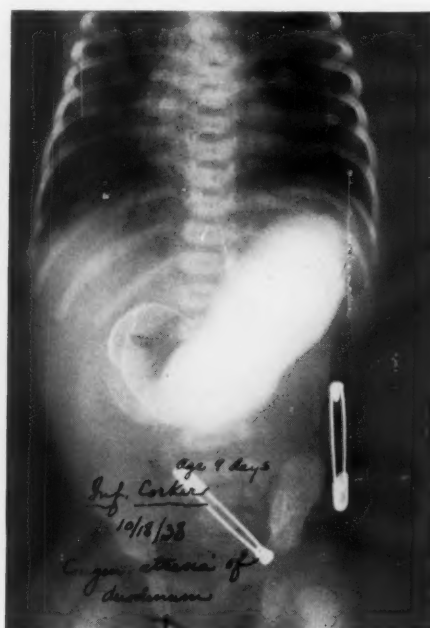


FIG. 11.—Case 13: Age nine days. Congenital obstruction of the third part of duodenum. Duodenojejunostomy (antecolic). Entero-enterostomy. Recovery.



tive for blood. (3) Cough and fever. Temperature  $100^{\circ}$ - $101^{\circ}$  F. December 13, 1935, barium by mouth. Roentgenograms showed that the barium began to leave stomach after two hours and emptied into a huge, dilated duodenum. *Operation*.—December 16, 1935: Baby has cough and fever  $102^{\circ}$  F. Right rectus incision. Huge dilatation of stomach and duodenum appearing almost like an hour-glass stomach. Deflated by needle

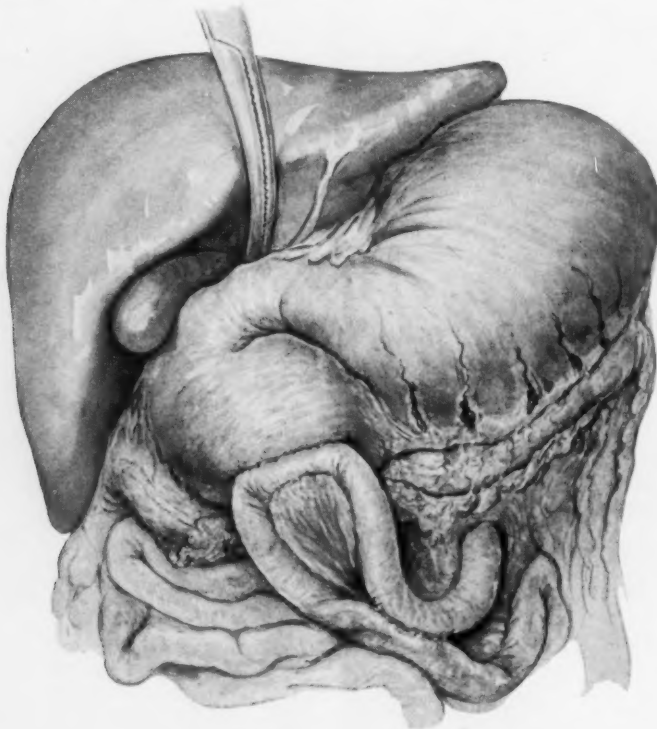


FIG. 12.—Case 13: Congenital obstruction of the third part of the duodenum. Duodenojejunostomy (antecolic). Entéro-enterostomy. Recovery.



FIG. 13.—Case 13: Age six months. Congenital obstruction of the third part of the duodenum. Duodenojejunostomy plus entero-enterostomy. Recovery. Excellent health six months later.

and syringe through wall of stomach. *Duodenojejunostomy*. December 17, 1935, death. Temperature  $106^{\circ}$  F. Pneumonia.

**Case 12.**—Mowcra, John, age five days. Birth normal, May 25, 1938. On second day began biliary vomiting. Jaundice. Obstipation. Physiologic icterus. Roentgenogram after barium showed none passed beyond dilated duodenum in seven hours. *Opera-*

# BOWEL OBSTRUCTION IN NEW BORN

tion.—June 3, 1938: Duodenum dilated down to crossing of superior mesenteric vessels. Jejunum collapsed. *Posterior gastro-enterostomy*. June 13, 1938, death. *Autopsy* (1) Bronchopneumonia—all lobes. (2) Icterus—neonatorum. (3) Incomplete rotation of colon. (4) Patent foramen ovale.

**Case 13.**—Infant Corker (Fig. 11), age nine. Normal birth at Cook County Hospital, October 9, 1938. Weight 5 lbs., 6 oz. Breast fed. On second day, began vomiting a chocolate colored, bloody material. Weight 4 lbs., 4 oz. Convulsion. From fifth day, after every nursing, biliary vomiting. No tumor palpable. October

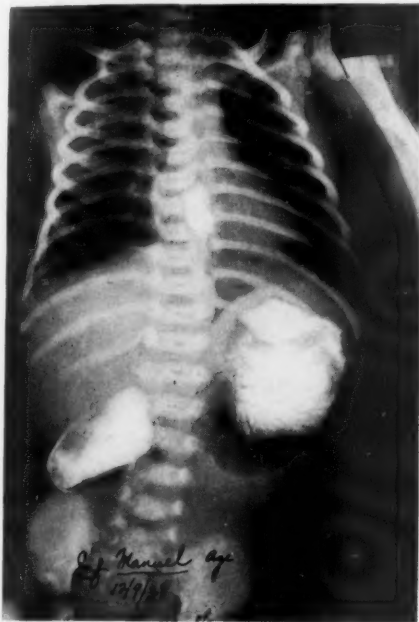


FIG. 14.—Case 14: Age eight days. Congenital obstruction of the third part of the duodenum. Duodenojejunostomy (transmesocolic). Recovery. Excellent health four months after operation.



FIG. 15.—Case 14: Age eight days. Congenital obstruction of the third part of the duodenum. Duodenojejunostomy (transmesocolic). Recovery. Excellent health four months after operation.

17, 1938, barium meal roentgenogram showed, complete obstruction at third part of duodenum, with dilatation. Few flecks of barium passed after three hours. *Operation.*—October 18, 1938; Local anesthesia. Duodenum dilated, 2 cm. wide, down to crossing of



FIG. 16.—Case 14: Age eight days. Congenital obstruction of the third part of the duodenum. Duodenojejunostomy (transmesocolic). Recovery. Excellent health four months after operation.

superior mesenteric vessels. Jejunum size of goose-quill. *Antecolic duodenojejunostomy* plus *entero-enterostomy*. Fine silk, two-row method. No clamps. Recovery (Figs. 12 and 13).

**Case 14.**—Infant Manuel (Fig. 14). Born at Cook County Hospital, December 2,

1938. Weight 7 lbs. Biliary vomiting since birth. Dehydration. December 8, 1938, weight 5 lbs., 8 oz. Visible epigastric peristalsis. Barium meal, December 9, 1938, showed complete obstruction of lower duodenum, with dilatation. Nothing passed after two hours. *Operation*.—December 10, 1939: (age eight days). Local anesthesia. Rectus incision. Dilated duodenum down to crossing of mesenteric vessels. Jejunum collapsed. *Duodenojejunostomy* (transcolic). Silk, two rows. Recovery (Figs. 15 and 16).

## CONCLUSIONS

(1) Progress in this field of surgery depends largely on the early diagnosis of the obstructive lesion and adequate preoperative preparation.

(2) The use of local anesthesia is strongly advised.

(3) If the atresia is in the jejunum or ileum simple enterostomy is useless. Adequate exposure and a short-circuiting lateral anastomosis offers the only hope of success.

(4) If the obstruction involves the duodenum, a gastro-enterostomy for those above the ampulla and a duodenojejunostomy for those below the ampulla are the procedures of choice. The addition of an entero-enterostomy between the afferent and efferent loops of the anastomosis, where there has been narrowing at the proximal end of the suture line (as in my Case 13), may make the difference between success and failure.

(5) Much depends upon the technical skill of the surgeon, and the use of the finest suture material is essential.

(6) All of these little patients demand the most painstaking postoperative care.

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denum better. Second, it prevents neutralization of the acid secretion of the stomach, and consequent loss of appetite. This proved very trying in one of our cases of gastrojejunostomy and was relieved only after a supplementary duodenojejunostomy had been performed. In stenosis of the duodenum the choice of operation is less important.

For cases of extrinsic duodenal obstruction due to faulty rotation, the operation first described by me, in 1932, and by Morton, in 1936, is the only operation which has proved satisfactory in our hands. There are three essential features to this operation: First, delivery of the whole midgut outside the abdomen; second, untwisting the volvulus when present (it has been present in most of our cases); and third, exposure of the duodenum through its whole course.

Much progress has been made in the last ten years. The prognosis depends on the condition of the patient, the condition of the bowel (whether there is necrosis or perforation), the skill of the surgeon, and the pre- and postoperative care. When Doctor Miller states that only three cases of jejunal or ileal atresia had been successfully operated upon, he must have overlooked some of the literature. In 1933, I reported three cases of my own successfully operated upon, and four from the literature. Since that time, we have had three more successful anastomoses for jejunal and ileal atresia. Again, Doctor Miller states that there have been only 16 cases of successful anastomosis for intrinsic duodenal obstruction. As I reported seven cases of duodenal anastomosis successfully operated upon at the Children's Hospital prior to 1937, which he has not mentioned, he must have missed this article, also. When Doctor Miller mentions that there have been only six cases of extrinsic duodenal obstruction relieved by operation, it is quite surprising.

TABLE I  
CONGENITAL INTRINSIC OBSTRUCTION OF DUODENUM

Operation	Number of Cases	Recov- eries	Deaths
Jejunostomy (for feeding) .....	1	0	1
Posterior gastro-enterostomy .....	2	1	1
Duodenojejunostomy .....	14	7	7
Total .....	17	8	9

CONGENITAL EXTRINSIC OBSTRUCTION OF DUODENUM

Ladd's operation .....	29	24	5
Total both types .....	46	32	14

In the extrinsic type of obstruction there were four additional cases which had various other types of operation which were unsuccessful.

Morton reported nine cases in 1936. I reported 19 in 1937, and Donovan 12 in January, 1939. At the present time at the Children's Hospital, we have had six cases successfully operated upon for jejunal or ileal atresia; nine for intrinsic duodenal obstruction, and 24 for extrinsic duodenal obstruction. Although the mortality is still higher than it should be, the picture is not quite so gloomy as Doctor Miller paints it, and I think the mortality should be very much lower in the next few years than it has been in the past.

Doctor Ladd then showed several slides demonstrating the following conditions:

A case of duodenal stenosis resulting from an intrinsic obstruction of the

third part of the duodenum, in which the duodenum was almost as large as the stomach.

A case of partial obstruction due to malrotation of the gut with a volvulus of about  $90^{\circ}$ , which was not sufficient to interfere with the circulation. Many of them had twisted more than one complete circle, and he recalled one which appeared to have had four complete turns. This was relieved by the operation which he had described; namely, of first untwisting the volvulus and then transferring the whole gut to the left side, exposing the duodenum throughout its whole course, which allows passage of food through the duodenum. He felt that this was an essential part of the operation for malrotation. The cases that had been operated upon by simply untwisting the volvulus have either all recurred or died. In other words, if one omits this part of the operation it is not successful.

A case of duodenal atresia in which the diagnosis was made without employing barium. With the stomach and duodenum so clearly demonstrated, plus not finding any cornified epithelium in the meconium, the diagnosis is absolutely positive, or as positive as any diagnosis ever is. This was relieved successfully by duodenojejunostomy.

The last case demonstrated was that of a three-day old infant who had vomiting from the first feeding. The plain film showed air in the stomach and also in a loop of bowel below. This was so confusing we took another film with the patient upside down, in the hopes that this would clarify the situation. Instead of clarifying it, however, it made it a little bit more confusing. This case was an atresia of the jejunum with an inadequate, and unattached mesentery, so that the air which was seen away down in the pelvis in the inverted position is the same air that was seen in the usual position of the stomach in the upright position. At operation, the blind end was beginning to become necrotic. About six or eight inches of the jejunum was resected, and a lateral anastomosis performed. The child had an uninterrupted convalescence and was discharged from the hospital on the fourteenth day.

DR. EDWARD J. DONOVAN (New York): We have been interested in this subject for a number of years, and in January of this year, Doctor McIntosh and I reported 20 cases of congenital duodenal obstruction from the Babies' Hospital in New York. Since that time I have operated upon five additional cases. The youngest child in this first group was 30 hours old, in whom we found a volvulus of the small intestine with complete gangrene of the jejunum at that point, and nothing, of course, could be done.

In the five cases operated upon since this first group was reported, we have found some very interesting conditions. The first patient was operated upon at the age of 24 hours. This baby was born with abdominal distention; had bilious vomiting almost immediately, and continuously after the cord was tied; passed no meconium in 24 hours. At operation it was found that he had a volvulus of the small intestine with gangrene and perforation of the jejunum, a process that I would think probably had been going on about two or three days.

One other case of this five, we found had an intrinsic lesion of the duodenum. We found also that the stomach was on the right side; the duodenum on the left; the liver was in normal position. The common bile duct passed into the stomach through the posterior gastric wall. This baby was operated upon at the age of five days, and died seven days later from aspiration pneumonia.

In one other case of this five, we had given barium for diagnosis and found

at operation a volvulus of the jejunum and also found that the barium had perforated the volvulus. Therefore, I would like also to call attention to the fact that it is very important to be careful about giving these babies barium. I think Doctor Ladd's suggestion that you can get almost as much information by a plain roentgenogram of the abdomen is very helpful. It was necessary in this baby to resect the intestine, and the child died.

We have had a great many cases of volvulus of the small intestine in the series reported, and we feel the volvulus occurs because the cecum and ascending colon have not attached themselves to the posterior abdominal wall. The last stage of rotation is fixation of the ascending colon in the right lower abdomen. If fixation does not take place, it leaves everything free to turn around the superior mesentery artery. We also attach the cecum and ascending colon to the right lower quadrant at operation believing that this prevents recurrence of the volvulus.

Doctor Donovan then showed lantern slides demonstrating other causes of congenital duodenal obstruction such as intrinsic lesions, volvulus and fixation of the duodenum in abnormal positions. He also showed slides of a case with complete reversal of rotation and duodenal obstruction.

DR. J. SHELTON HORSLEY (Richmond, Va.): Doubtless many infants die from this disease because it is unrecognized. I have had three cases of congenital occlusion of the duodenum, all of them operated upon within the first seven days. Two of these cases were reported in the Virginia Medical Monthly for June, 1935. In two of them a posterior gastro-enterostomy was performed. In the other, a duodenojejunostomy was performed. One recovered and is now well; one died of pneumonia; and one of shock four hours after operation. The diagnosis between congenital pyloric stenosis and occlusion has been clearly explained by Doctors Miller and Ladd.

So far as I know, these cases are the only ones that have been reported of operation for congenital, complete atresia of the duodenum in the State of Virginia, and all of them came from one town, Newport News, where there are some excellent pediatricians. It is not at all probable that they are the only cases of this kind in Virginia. The fact is that, in all human probability, many of these cases are simply treated for improper feeding, the formula changed, and they die. The mortality from this lesion must be very considerable.

As Doctor Miller has insisted, the sutures must be of fine material. It is quite different from operating upon an adult. The tissues are very thin, and if the transverse colon is lifted up, the mesocolon is transparent and can be almost disregarded, as long as the vessels are not injured. Two tractor sutures of fine silk are placed between the jejunum and the stomach, and are held taut without any clamps on the wound, because they are unnecessary, are in the way, and there is practically no chance of infection from the stomach or upper jejunum in an infant that young. An incision is made half an inch long, and the posterior margin of the stomach is sutured to the posterior margin in the jejunum with a continuous suture of fine silk. That is continued anteriorly and tied to the original end. Anteriorly another row of sutures is placed; that is all that is necessary.

DR. PHILEMON E. TRUESDALE (Fall River, Mass.): It is my feeling that Doctors Miller and Ladd and a few others merit the highest commendation for the work which they have done in this field. My interest was aroused during a visit to Cook County Hospital, Chicago, six months ago. I saw Doctor Miller's cases in the convalescent stage. He showed me the records of seven cases upon which he operated successfully.

On November 8, 1938, an infant one month old, weighing four pounds and ten ounces, was admitted to our hospital. It was said that the birth weight was three pounds. Vomiting, which occurred daily since birth, became more frequent. The infant was anemic, emaciated, and dehydrated. An effort was made to establish a fluid balance; 20 cc. of citrated blood in normal salt solution were given intravenously. A roentgenogram demonstrated the point of obstruction to be in the transverse portion of the duodenum. After a period of preparation on behalf of the patient, on November 16, a duodenojejunostomy without the use of clamps was performed. My chief difficulty during the operation was from hemorrhage. It seemed to me that my hemostasis should have been better, and I was surprised that the little patient survived the operation. To expediate the operation some form of tiny intestinal clamp might be employed.

Last night Doctor Wilkie and I improvised a pair of miniature clamps which we describe as the hairpin clamp. It is made of two ordinary hairpins of the "bobby" type. The two pins are fastened side by side with a ligature of silk, and are held in position by a small hemostat attached across the blunt ends of both hairpins. As the pin is constructed, the outer phalange has a slight but sufficient amount of pressure to control bleeding. The parts of the clamp are simple to assemble, easy to improvise, and very useful in conserving the blood volume for these feeble infants.

DR. EDWIN M. MILLER (Chicago): I do not want to prolong this discussion unnecessarily but I do wish to thank those who have taken an interest in discussing this paper. I also want to apologize to anybody anywhere if I have inadvertently overlooked some article they have written on this subject.

I have read very carefully, not only once but several times, the articles of Doctor Ladd published in 1932 and 1937, and I have picked out from those in which he has given details of the cases, the ones which I was sure, without any question of doubt, were cases of complete obstruction, operated upon a few days after birth. We all know there have been a large number of cases reported in the literature of partial obstruction, and I have not attempted, of course, to include those in this series.



## PEPTIC ULCERS PERFORATING INTO THE PANCREAS \*

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THE STATUS of peptic ulcer of the duodenum has changed within the last 20 years. Formerly, a peptic ulcer anywhere was often considered to be a surgical lesion, and operations, especially posterior gastro-enterostomy, were the routine therapy. Lewisohn reported recurrent ulcers, usually jejunal ulcers, in about 34 per cent of the cases of gastro-enterostomy from the clinic with which he was associated. Church and Hinton found in a study of peptic ulcer that after gastro-enterostomy there were numerous complaints; only 37 per cent of the patients were free from symptoms, and 16.4 per cent had marginal ulcers. It is now fairly generally agreed among surgeons who have had much experience in gastric surgery that about 80 per cent of *duodenal* peptic ulcers may be cured by proper medical treatment. It has been established that medical treatment consists not only in diet and the administration of alkalis, but in lessening worry and nervous tension, for peptic ulcers are frequently found in high-strung, nervous individuals, although occasionally they occur in the phlegmatic. They have been found in infants.

The cases operated upon are what might be termed residual cases of duodenal peptic ulcer that resist medical treatment or that develop some complication as perforation, repeated or massive hemorrhage, or obstruction.

*Gastric* peptic ulcers, however, are in another therapeutic class, because in a definite proportion of gastric peptic ulcers cancer develops, and even if the ulcer is cured the scar may remain a point of irritation.

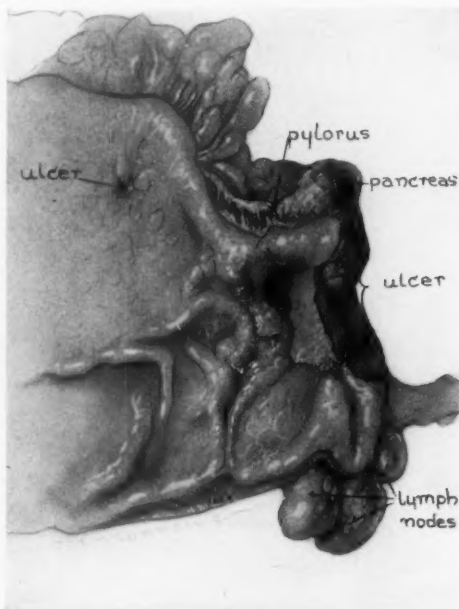
A peptic ulcer that has perforated into the pancreas presents quite a different clinical and pathologic picture from an ulcer that has not so perforated. It always gives a history of previous gastric disturbance, which may be long or short.

Relief by food, soda or vomiting is not constant and there is a sense of discomfort and a tenderness on pressure in the upper abdomen which was not present before the perforation. When the perforation actually occurs pain may be severe.

Medical treatment after the perforation is not so effective as before the perforation. There is also considerable danger of bleeding. The vascular tissues of the pancreas tend to bleed quite freely, particularly if the perforation is large, and the hemorrhage may be profuse. A posterior perforating ulcer of the pyloric sphincter gives added symptoms of discomfort and obstruction because of the spasm of the sphincter and local edema. Roentgenologic examination is not always convincing, especially if the ulcer is within the grasp of the pyloric sphincter.

\* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

The pathologic picture also changes, because, in addition to the lesion in the stomach, there is some degree of pancreatitis. The pancreatitis is usually local around the region of the perforation, but it may become more extensive. Unless it spreads, the associated local pancreatitis gives no symptoms of a disturbed function of this gland and laboratory tests are futile. The pain is often referred to the back, either to the right or to the left of the spine, and is occasionally so intense as to resemble the pain caused by a stone in the kidney, by nephralgia, or by acute cholecystitis. The previous history of the patient with peptic ulcer should aid much in the diagnosis of the subsequent events when there is perforation into the pancreas.



**Case 1.**—As an illustrative case: Mrs. J. H. A., Path. No. 13684, white, age 48, was admitted to the hospital, July, 1938. The gallbladder containing a stone, had been removed elsewhere ten years previously. The patient, however, continued to suffer with indigestion. On admission the symptoms of pain and discomfort pointed to the back and to the right kidney, so a gastro-intestinal roentgenologic examination was not made, but a complete urologic study was made. The right kidney was enlarged and somewhat prolapsed. There was slight pain in the epigastric region, though this was not marked. The diagnosis of nephralgia seemed probable. On opening the abdomen for exploration a duodenal ulcer, which had perforated into the upper part of the head of the pancreas, with inflammatory involvement of the surrounding tissues, was found (Fig. 2). A partial gastrectomy was performed and the patient recovered

FIG. 2.—Path. No. 8462: W. G. M., white, male, age 66. Specimen of stomach measured 10 cm. on the lesser curvature and 17 cm. on the greater curvature.\* Much of the gastric mucosa was congested. There was a gastric ulcer about 5.5 cm. from the pylorus on the lesser curvature, and within the grasp of the pyloric sphincter was a deep oblong ulcer which had perforated into the pancreas. There were large lymph nodes on the lower border of the stomach. A Hofmeister operation was performed June 11, 1929, and a layer of pancreatic tissue was excised with the base of the ulcer. The patient is now entirely symptom-free, and says (April 4, 1939) that he has "had no pain since leaving the hospital, ten years ago." There were only two Hofmeister operations in this series of cases.

\* The anatomists are reluctant to commit themselves about the measurements and capacity of the stomach because it varies so much, but Jackson, in Morris's Human Anatomy, 9th edition, states that the lesser curvature of the stomach averages about 10 cm. (7.5 to 15 cm.), and that the greater curvature is three or four times as long.

In these specimens there is usually about 2 cm. of a cuff of duodenum attached, which makes the length along the curvatures appear larger.

with complete relief of her symptoms. Under date of April 7, 1939, she reports, "I can eat almost anything without discomfort. Before the operation I was suffering intense pain all the time, but now I am free from pain and have gained 21 pounds."

Not infrequently, in cases of persistent pain or discomfort unrelieved by medical treatment when a peptic ulcer has been demonstrated in the anterior wall of the duodenum, there exists in the posterior wall another ulcer that has

perforated into the pancreas. One should not be deceived, then, by an ulcer in the anterior wall of the duodenum into thinking that it is the only lesion.

After sifting the cases that are not cured by medical treatment, Hinton reports on adherent posterior duodenal ulcers and states that for the past four years and nine months the operation he has performed for all duodenal ulcers has been a subtotal gastrectomy. He emphasizes the fact that the inflammatory lesion itself should be removed, and if this is done primarily the mortality rate is lowered. In 48 primary subtotal resections there were two deaths, a mortality rate of 4.1 per cent. In 16 secondary gastric operations there were five deaths, a mortality rate of 31 per cent. In the entire series of 64 cases there were seven deaths, with a mortality rate of 10.9 per cent.



FIG. 2.—Path. No. 13684: J. H. A., white, female, age 48. Specimen of stomach measures 15 cm. along the lesser curvature and 18 cm. along the greater curvature. At the upper posterior part of the duodenum is a prolongation of the duodenum which is covered with pancreatic tissue removed. The insert shows the internal view of the ulcer which had penetrated into the pancreas.

#### CASE REPORTS

During a period of ten years, from December 31, 1928, to December 31, 1938, I have operated upon 20 cases of peptic ulcer of the stomach or duodenum that had perforated into the pancreas. In all of these cases a partial gastrectomy was performed, in 18, by a modification of the Billroth I type described elsewhere, in which the upper border of the stomach is united to the upper border of the duodenum and the duodenum is flared open. In two cases this operation could not be applied, and a Hofmeister modification of the Billroth II type was performed.

Nine of the ulcers were duodenal, nine were gastric, one was a duodenal-jejunal ulcer, and in one case there were both a duodenal and a gastric ulcer. Five of the gastric ulcers were within the grasp of the pyloric sphincter.

# PEPTIC ULCERS

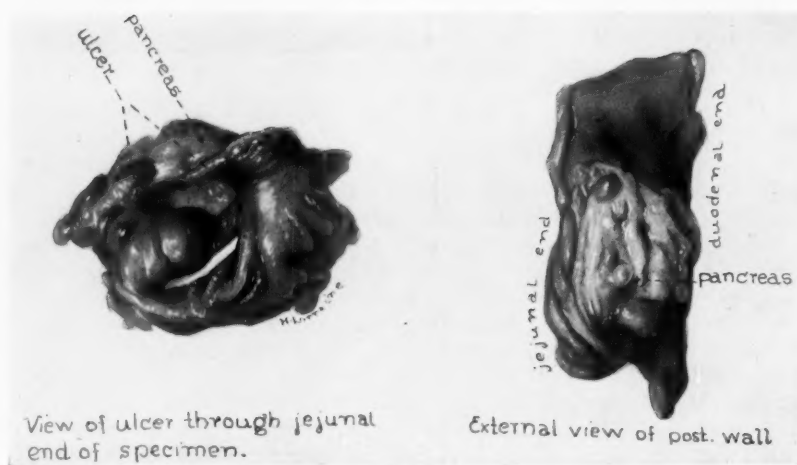


FIG. 3.—Path. No. 9247: L. E., white, male, age 46. Section of specimen showing the terminal duodenum and the first part of the jejunum together with the base of the ulcer which had perforated into the pancreas. On the right there is a posterior view showing the pancreatic tissue that was removed along with the specimen.

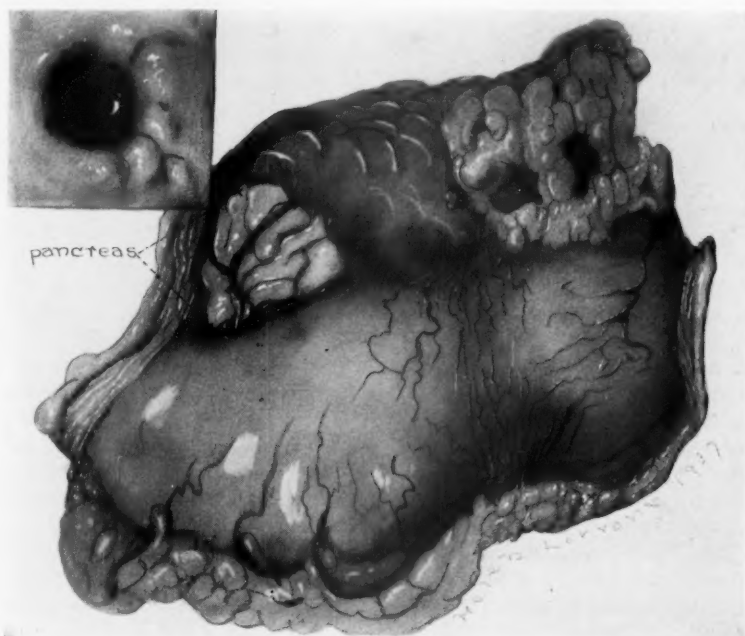


FIG. 4.—Path. No. 12755: D. D., white, male, age 69. Operation February 17, 1937. The specimen of the stomach measures 10.5 cm. along the lesser curvature and 15 cm. along the greater curvature. In the upper posterior wall, about 2 cm. from the cardiac end of the specimen, is an excavating ulcer 1.75 cm. in diameter. The specimen shows a layer of pancreatic tissue which has been removed with the ulcer. The insert shows the interior view of the ulcer. The patient reported, April 3, 1939, that he is "completely cured. I have not been sick a day since I left the hospital."

The only death in this series of cases was of a patient in whom it was impossible to remove the ulcer. A Hofmeister operation was performed. A report of this case is as follows:

**Case 2.**—Path. No. 11695: T. B. B., white, male, age 39, had a history of several massive hemorrhages from the stomach and the passage of tarry stools. One hemorrhage occurred March 5, 1935, and on March 22, there was another large hemorrhage. An analysis of the gastric juice showed the HCl 56, with total acids 78. The hemoglobin was 25 per cent, red blood cells 1,520,000, and white blood cell count 5,200. March 23, a partial gastrectomy was performed. In the posterior wall of the duodenum there was an ulcer, so large that it could not be removed. It began about two centimeters from the pylorus and penetrated into the head of the pancreas. It was not bleeding then, but the base was necrotic. It extended to a point near the ampulla of Vater. The upper sides of the ulcer were undermined with a cautery in order to close the duodenum, and a Hofmeister operation (Billroth II) was performed. The patient was given a transfusion of blood. He did well for eight days, when he had a sudden attack of intense pain and his blood pressure sank to 70 systolic. It was thought that there was a perforation. He was given another transfusion, and under local anesthesia the abdomen was opened. No evidence of peritonitis could be found. There was a large mass about the head of the pancreas. A jejunostomy was performed for feeding. The patient died the following day. Necropsy showed the general peritoneal cavity about normal, with no free fluid. The suture line involving the union of the stomach and jejunum and the enterostomy were in good condition. The lesser peritoneal cavity which had been walled-off by adhesions was filled with thin pus. The infection probably came from the large ulcer through the lymphatics. The ulcer involved much of the head of the pancreas. In the center of the ulcer was a large vein, the midportion of which had been destroyed. Both ends of the vein were occluded with a well organized thrombus. The quick development of the infection simulated a perforation into the peritoneal cavity.

There was one case of ulcer diathesis, in which there were recurrences after operations performed elsewhere and by me. Medical treatment afforded no relief.

**Case 3.**—Path. No. 9247, L. E., white, male, age 46, gave a history of having been operated upon elsewhere in 1922; a gastro-enterostomy was performed. One and one-half years later, there was an excision of a recurrent ulcer and separation of adhesions. Another operation for adhesions was performed, then a pyloroplasty, and finally another gastro-enterostomy was performed. He was admitted to St. Elizabeth's Hospital in August, 1930. Analysis of the gastric juice showed HCl 55, with total acids of 67. In the terminal duodenum and the first part of the jejunum there was an extensive ulcer that had perforated into the pancreas. The gastro-enterostomy was disconnected, the segment of affected bowel was dissected from the pancreas with a cautery, resected, and an end-to-end union was made with much difficulty; a partial gastrectomy of the modified Billroth I type was then performed (Fig. 3). Four days later, because of obstruction at the site of the intestinal resection, a jejunostomy was performed. After this, the patient made a fairly satisfactory recovery and the obstruction disappeared, but six months later he had symptoms of a recurrent ulcer. He was operated upon again. There was a large anterior perforated ulcer involving the stomach, duodenum and colon. The perforations were closed, but the patient gradually sank and died eight days later.

This case is not the usual type of case being considered, for it was a perforation of the terminal part of the duodenum along with the jejunum and it occurred after several previous operations performed elsewhere, but it is included because the duodenum was involved.



## PEPTIC ULCERS

These cases of ulcer diathesis are, fortunately, rather rare, but they are extremely puzzling. It seems radical, but after all other means fail a total gastrectomy might be considered. The two cases that had recurrent symptoms after partial gastrectomy are appended:

**Case 4.**—Path. No. 12130: R. E. C., white, male, age 47. The patient suffered intensely. The gastric juice showed HCl 18, total acids 38. January 10, 1935, a partial gastrectomy was performed for a posterior perforating ulcer, which was chiefly in the duodenum but extended into the grasp of the pyloric sphincter.<sup>5</sup> There was much inflammation and infiltration around this ulcer. He made a fairly satisfactory recovery, but a few months later began having further symptoms, and in February, 1936, he was again operated upon. There was an extensive inflammatory exudate about the junction of the stomach and



FIG. 5.—Path. No. 13488: R. E. M., white, male, age 41. Partial gastrectomy April 9, 1938. The specimen of the stomach measured 11 cm. along the lesser curvature and 17 cm. along the greater curvature. The distal half showed evidence of gastritis with some punctate erosions. In the lower posterior portion of the duodenum there was a perforating ulcer measuring 1.25x0.75 cm. which involved the pancreas.

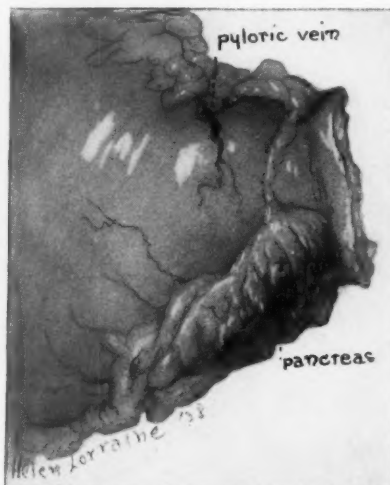


FIG. 6.—R. E. M. Posterior surface of the specimen shown in Figure 5, with the pancreatic tissue attached. In the lower portion, and just beneath the ulcer in the pancreas, were several large vessels from which the hemorrhage probably came.

duodenum. No effort was made to disturb these adhesions, but when the stomach was opened for a gastro-enterostomy the interior was explored with the finger. An ulcer, apparently about two centimeters in diameter, could be palpated on the lower and somewhat posterior portion of the stomach near the site of the previous resection. There was a wide opening between the stomach and duodenum. The ulcer did not appear to be malignant. A posterior gastro-enterostomy was performed, with a temporary jejunostomy for feeding. He made a satisfactory recovery. Under date of April 5, 1939, he reports: "I am entirely free from any symptoms of stomach trouble whatsoever."

**Case 5.**—Path. No. 13488: R. E. M., white, male, age 41, had had a perforated duodenal ulcer from which there had been two massive hemorrhages and which did not respond to medical treatment. There had been symptoms for two or three years. The patient was high-strung and nervous. The gastric juice showed HCl 70, and total acids 98. A partial gastrectomy with removal of the adherent part of the pancreas was per-

formed April 9, 1938. The ulcer was in the lower, posterior portion of the duodenum and measured 1.25x0.75 cm. There was gastritis with a few punctate erosions in the pyloric portion of the stomach (Figs. 5 and 6). The patient made a satisfactory recovery and was well for a while, but the discomfort recurred, though there was no further hemorrhage and the symptoms were not so severe as before the operation. He was again operated upon November 10, 1938. There was extensive reaction about the site of the anastomosis of the stomach and duodenum. The stomach was drawn up high and was rather small. A posterior gastro-enterostomy was performed. Exploration of the pyloric end of the stomach could not be made, but from the surrounding inflammation and exudate, it seems probable that he had a recurrent ulcer. He reported in April, 1939, that he is now symptom-free.

In these two cases of failure to permanently relieve the clinical symptoms, apparent cure has been obtained by a secondary operation of gastro-enterostomy. Both of these patients were nervous and high-strung men, a type apt to have a recurrence of ulcer after any gastric operation. It would seem better to have performed a primary partial gastrectomy, by which the patient was temporarily relieved, and a gastro-enterostomy later, than to have performed

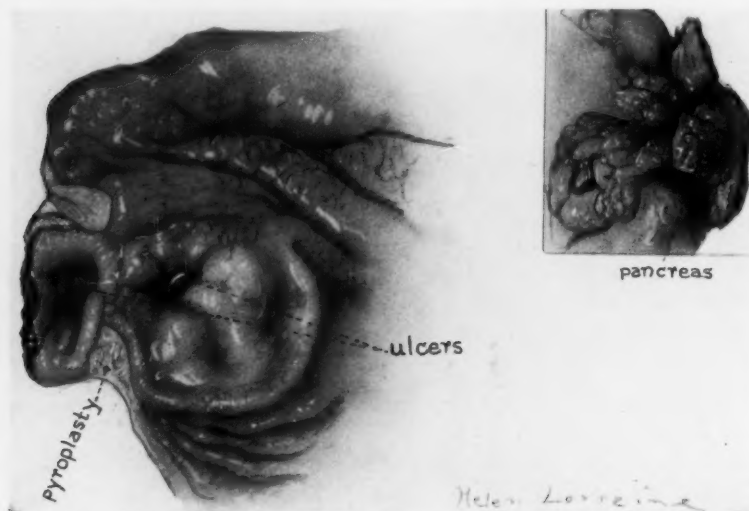


FIG. 7.—Path. No. 12831: A. V. H., white, male, age 52. Operation April 27, 1937. Specimen of the stomach measured 16 cm. along the lesser curvature and 25 cm. along the greater curvature. On the posterior surface of the stomach near the pyloric sphincter was some adherent pancreatic tissue which was dissected off with the cautery. The stomach showed evidence of gastritis and there was a pouch, probably resulting from a preceding pyloroplasty. There were two peptic ulcers, one in the stomach and one in the duodenum.

a primary gastro-enterostomy, with the probability in these two cases of a secondary jejunal ulcer which would involve the more difficult subsequent procedure of taking down the gastro-enterostomy and resecting the stomach.

There are two patients who may be classed as improved but not cured by the partial gastrectomy:

**Case 6.**—Path. No. 12831: A. V. H., white, male, age 52, was operated upon June 30, 1928. A gastro-enterostomy, which had been performed elsewhere six years previously, was disconnected, and a pyloroplasty was performed. The patient did fairly well

## PEPTIC ULCERS

for seven years, then he had a lesion about the pyloric portion of the stomach. The gastric juice showed HCl 37, total acids 57. A partial gastrectomy was performed, April 27, 1937. There were two peptic ulcers, one in the stomach and one in the duodenum. Both had perforated into the pancreas, and in both there was a base of pancreatic tissue attached to the specimen (Fig. 7). He reports now that he is better, though he still has some gastric symptoms, but is "taking life easy" and is fairly comfortable.

**Case 7.**—Path. No. 13512: V. C. T., white, male, age 51, had a large ulcer of the pyloric portion of the stomach penetrating into the pancreas. The gastric juice showed HCl 50, and total acids 60. He made a satisfactory recovery from a partial gastrectomy performed April 22, 1938, but at present states he has gastric symptoms, unless he ad-

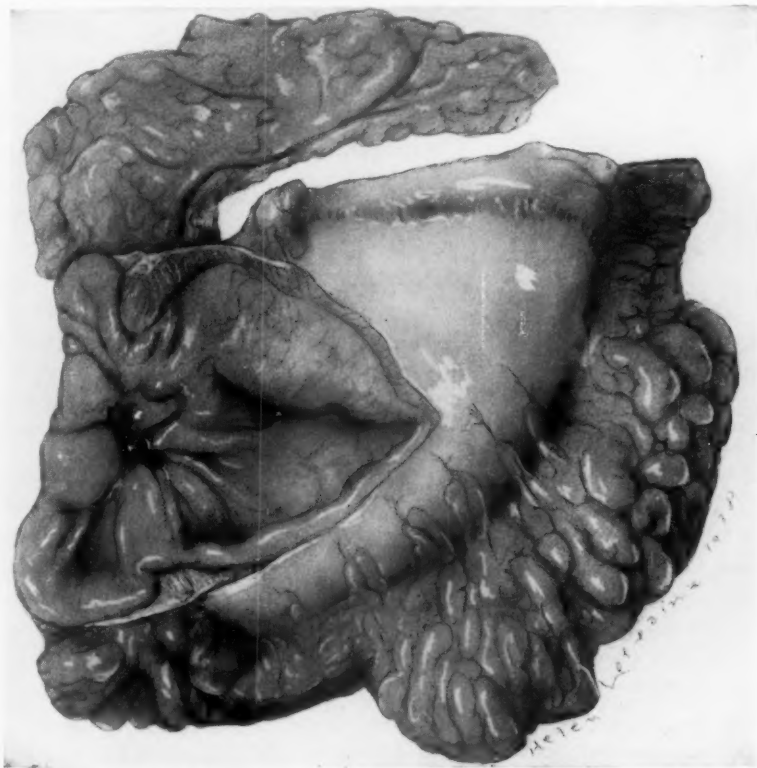


FIG. 8.—Path. No. 13993: D. N. S., white, male, age 50. Partial gastrectomy December 19, 1938. Specimen of the stomach measured 6 cm. along the lesser curvature and 16 cm. along the greater curvature. On section, there was a deeply perforating ulcer in the upper posterior part of the pyloric sphincter, more on the stomach side than on the duodenal. It measured 0.5x1 cm. Attached posteriorly, was a segment of pancreatic tissue into which the ulcer had perforated. The patient reported April 3, 1939, that he was free from symptoms and "feeling better than I have felt for a long time."

heres closely to an ulcer diet. He may be classed as improved. In his history, taken before the operation, the following significant paragraph appears: "He has always been a gluttonous type of eater, and tells of eating as many as 10 or 12 biscuits at a meal, of drinking rather heavily at times in the past, and other such severe insults to his gastrointestinal tract."

An ulcer of the stomach perforating into the pancreas may resemble a peptic ulcer clinically and even in gross appearance and yet be malignant.

**Case 8.**—Path. No. 10792: C. G. W., white, male, age 31, had high acid values in the gastric juice (HCl 74 and total acids 86), and marked gastric symptoms. A partial gastrectomy showed two ulcers in the pyloric portion of the stomach; one had perforated into the pancreas. Grossly, they resembled very closely peptic ulcers, but microscopically, they proved to be small cell carcinoma. There was a recurrence of extensive carcinoma and death within nine months.

In addition to the cases herewith reported, in which a peptic ulcer perforating into the pancreas was demonstrated in the specimen removed, there were three patients with what appeared to be a duodenal ulcer perforating into the pancreas upon whom a posterior gastro-enterostomy was performed after loosely tying off the pyloric end of the stomach. These patients recovered satisfactorily. There were dense adhesions with an extensive exudate into the surrounding tissues, and the duodenum was fixed to the pancreas. However, this marked inflammatory reaction may have been from an accompanying duodenitis. The tissues were so welded together by firm lymphatic exudate that partial gastrectomy would have been unduly dangerous. As these lesions could not be demonstrated to be posterior perforating ulcers, they are not included in this list.



FIG. 9.—D. N. S. Posterior surface of specimen shown in Figure 8, with the pancreatic tissue attached.

The intense reaction in such instances would seem, too, to indicate a high resistance and a probability of recovery if some help is afforded by diversion of the gastric contents and by giving the tissues rest by ligating the pyloric end of the stomach just tightly enough to occlude without strangulation. Doubtless, the chronic cases, in which the lesion remains, have not sufficient resistance for healing, and it becomes necessary to remove the lesion (Table I).

**Treatment.**—The technic used in all but two of these cases is essentially the same as that previously described in several publications. It is a modification of the Billroth I type of operation in which the lesser curvature of the stomach is aligned to the upper border of the duodenum, and the duodenum is flared open to prevent obstruction. However, the procedure has to be altered somewhat in individual cases. After dividing and tying the segments of the gastrocolic omentum from the point of the proposed resection to the pylorus, and the vessels along the lesser curvature in the gastrohepatic omentum, the portion of the stomach to be removed remains attached only by its two ends and by the adherent ulcer. Two Payr clamps are placed on the body of the stomach, which is divided between them with an electric cautery. Usually the lesion will prevent the placing of a clamp on the duodenum. The stomach is then lifted up, and, with a very hot electric cautery, the adherent pancreas is shaved off as a thin slice, care being taken not to open the ulcer. This can best be done by approaching the adherent region carefully and freeing it to some extent on each side. Too much of the pancreas should not be removed (Fig. 10). If the ulcer is accidentally opened, the opening is plugged with

TABLE I  
SYNOPSIS OF 20 CASES OF PARTIAL GASTRECTOMY FOR PEPTIC ULCER PERFORATING INTO THE PANCREAS  
*December 31, 1928, through December 31, 1938*

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PEPTIC ULCERS

No.	Date	Sex		Location	Previous Operations for Ulcer	Operation		Subse- quent Gastro- enter- ostomy	Result				
		M.	F.			Mod. Bil. I	Hof.		Well	Imp.	Re- cured	Died	
1	6-11-29	M.		Duodenum	(1) Gastro-enterostomy.								
2	8-8-30	M.		Duo.-jej.	(2) Exc. rec. ulcer. (3) Pyloroplasty. (4) Gastro-enterostomy	x	x			x		x	
3	10-30-30		F.	Duodenum		x				x			
4	10-21-31		F.	Stomach		x				x			
5	9-16-33	M.		Stomach	Sut. perf. ulcer 1 yr. before, elsewhere	x				x			
6	8-11-34	M.		Stomach		x				x			
7	11-7-34		F.	Duodenum		x				x			
8	1-10-35	M.		Stomach		x				x			
9	3-23-35	M.		Duodenum			x						x
10	10-12-36	M.		Duodenum		x				x			
11	2-17-37	M.		Stomach		x				x			
12	4-2-37	M.		Stomach		x				x			
13	4-27-37	M.		Duodenum and stomach	(1) Gastro-enterostomy. (2) Pyloroplasty	x					x		
14	5-17-37	M.		Duodenum		x				x			
15	4-9-38	M.		Duodenum		x				x			
16	4-22-38	M.		Stomach		x						x	
17	7-15-38		F.	Duodenum		x				x			
18	8-15-38	M.		Duodenum		x				x			
19	10-21-38	M.		Stomach		x				x			
20	12-19-38	M.		Stomach		x				x			
Totals.....		16	4			18	2	2	16	2	1	1	

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wet gauze or the finger is inserted into it. Then, with tension on the stomach, the rest of the adherent strip of pancreas is cut off. If the cautery is quite hot and the stomach is lifted up, a thin slice of the pancreas can be quickly removed without burning one's finger. If the ulcer is in the stomach, after freeing it, the duodenum is separated from the pancreas and cut across with the cautery, catching the margins of the duodenum as the incision is made. The duodenal contents are removed with a suction apparatus and a sponge moistened with salt solution is gently placed in the duodenum. If the perforation is from a duodenal ulcer, the base of the ulcer is shaved off in a similar way. The operation here is somewhat more difficult because of the shortness of the stump of the duodenum, but this technic can be carried out,

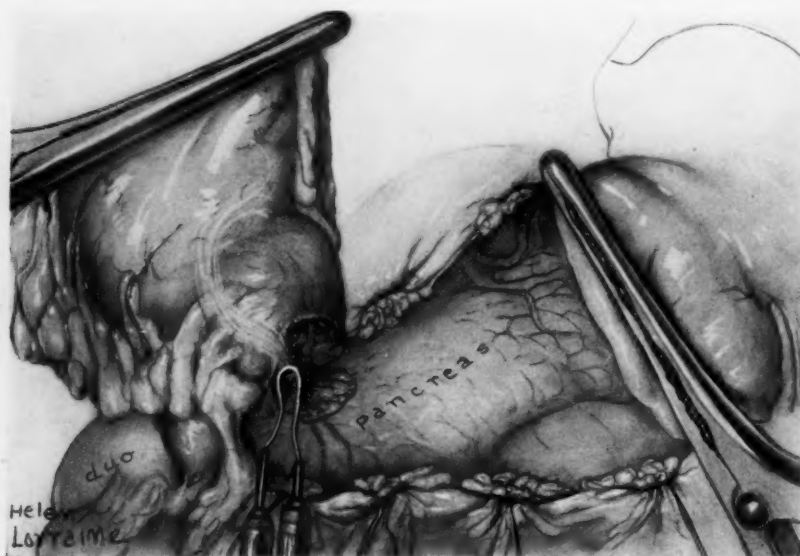


FIG. 10.—The stomach has been divided between two Payr clamps and the distal end is lifted up while the slice of pancreatic tissue which forms the base of a penetrating ulcer is being shaved off with the hot electric cautery.

probably more satisfactorily, in these cases than the Billroth II type of partial gastrectomy if the ulcer is removed, because with a very short stump of the duodenum resulting from the excision of the ulcerated area it becomes difficult to close the stump of the duodenum effectively. If there is back pressure, which occurs not infrequently after the Billroth II operation, a duodenal fistula may result, whereas in this type of operation the posterior wall of the stump of the stomach is tucked in by the short posterior wall of the stump of the duodenum and sutured. This makes the situation in this region comparatively safe because the wound in the pancreas has been made with the cautery and is sterile, and the peritoneum on the posterior surface of the stomach will readily unite to the short posterior stump of the duodenum and the denuded pancreas. Then, too, this sutured area is over the solid surface of the pan-

# PEPTIC ULCERS

creas, and if there is not an accurate healing at this point the charred and sterile pancreatic wound will act as a bumper of safety.

*A Stab Wound Gastrostomy.*—To give the stomach postoperative rest, it is essential that the contents of the stomach be removed and dilatation prevented, which is usually accomplished by the insertion of a Jutte or Levine tube into the stomach through the nose. In some patients the presence of the tube is quite a nuisance. If it stays in constantly for a few days it often irritates the

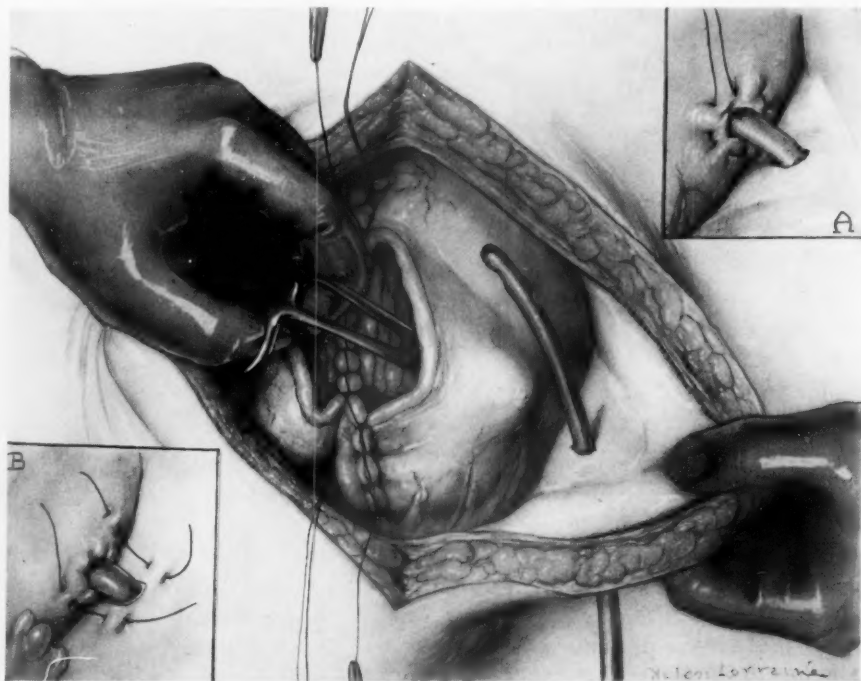


FIG. 11.—The first stage of a tube gastrostomy. After uniting the posterior margin of the stump of the stomach to the posterior margin of the stump of the duodenum, a sharp hemostat is thrust through the anterior wall of the stomach near the greater curvature. It grasps the end of a soft rubber catheter in which there is an additional perforation, and draws it into the stomach. The catheter may be introduced through a stab wound to the left of the incision before this is done, or it may be clamped at its middle and after being drawn into the stomach the butt end can be carried through a stab wound in the abdominal wall after the stomach and duodenum have been sutured together.

(A) After drawing about three inches of the catheter into the stomach the catheter is fastened to the stomach with a single suture of fine chromic catgut, and a purse-string suture is placed around the catheter.

(B) The stomach is being pulled snugly to the anterior parietal peritoneum. A few sutures of fine chromic catgut are placed, after which a tag of omental fat is fastened around the tube.

nose and throat, and if it has to be inserted every few hours, the repeated insertions are even more disagreeable than having the tube remain. Recently, I have employed a gastrostomy, which is much more comfortable to the patient and more efficient for drainage than the nasal tube. This is done as follows:

After the posterior row of sutures uniting the stomach to the duodenum is placed, a sharp-pointed hemostat is thrust (directly, not obliquely) through the stomach from within outward at a point on its anterior wall near the greater curvature, where the stomach can be easily brought into contact with

the abdominal wall. A soft rubber catheter, No. 18, in which an additional perforation has been made near the end, and which is clamped at its middle, is caught with the hemostat and drawn into the stomach (Fig. 11). After three or four inches of the catheter are within the stomach, the catheter is fastened to the gastric wall by a suture of fine chromic catgut and a purse-string suture of chromic catgut is placed around it. The butt of the catheter is drawn through a stab wound in the abdominal wall, and then clamped, and the clamp on its middle is removed. The catheter is gently pulled upon until the stomach is in contact with the parietal peritoneum. Sutures of fine chromic catgut are placed between the stomach and the parietal peritoneum and some omental fat is brought around this point of contact (Fig. 11B). The fat not only adds to the security of the punctured wound, but may prevent a subsequent tight adhesion.

By this method the muscular layers of the stomach are not cut, as would occur if a knife were used to make the puncture; their fibers are merely pushed apart as are the muscular bundles of the abdomen in making a McBurney incision. The catheter fits in snugly, and there is usually no leakage after the catheter has been removed.

#### CONCLUSIONS

There seems to be some danger of rather extensive pancreatitis from an ulcer that has perforated into the pancreas. With the base of the ulcer consisting of pancreatic tissue, if the operation is delayed too long it may well be that the residual pancreatitis will not clear up promptly.

The advantages of this procedure are that: The ulcer is removed along with the superficially infected portion of the pancreas; the stomach empties physiologically into the duodenum, which is more resistant to the gastric juice than the jejunum; the region of trauma is limited to one field, and if there is a recurrent ulcer a posterior gastro-enterostomy can readily be performed. A primary gastro-enterostomy, which leaves this lesion *in situ*, does not appear to be logical, though there may be circumstances in which it is the only operation indicated, as when the reaction around the ulcer is extensive.

The mortality rate should not be great. In these patients, in which this type of operation has been performed, there has been no operative death. The only death following operation was in a patient in whom this procedure was not possible because of the extent of the ulcer. The ulcer could not be excised, and the Hofmeister-Billroth II type of operation had to be performed.

A simple method of making a gastrostomy to substitute for using the nasal tube is described.

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DISCUSSION.—DR. JOHN M. T. FINNEY, JR. (Baltimore, Md.): I feel that there are two points in stomach surgery which Doctor Horsley's procedure calls to our attention immediately. The first is the now pretty well recognized principle of the necessity of resection of the stomach in these cases of ulcer perforating into the head of the pancreas, the necessity resting principally on the control of hemorrhage.

It has been shown by a great many people that because of the location of the main vessels in the blood supply to the pylorus and the upper duodenum, these ulcers perforating into the head of the pancreas are prone to hemorrhage, and hemorrhage of severe proportions, and that it is almost impossible to obliterate these vessels, to properly tie them and control the hemorrhage thereby, unless one resects the stomach.

Of course the resection of the stomach accomplishes another thing, also, and that is, providing the resection is extensive enough, the removal of a sufficient quantity of the acid bearing area of the stomach to materially reduce the free acid after the operation and thereby control, at least to a certain extent, the recurrence of marginal ulcers following the resection.

The second principle is, I think, probably much more debatable than the first: What type of anastomosis one is going to perform following the resection. We feel, as does Doctor Horsley, that, where it is possible to maintain the normal anatomicophysiologic basis, anastomosis of stomach to duodenum, it is much more preferable than the anastomosis of stump of stomach to jejunum. This is not always possible, but where it is possible, I feel, as I am sure Doctor Horsley does, that one can reduce materially the incidence of postoperative marginal ulceration.

I do not altogether agree with Doctor Horsley on the method of this anastomosis. Personally, I much prefer an end-to-side anastomosis into the stump of the duodenum, having closed the stump, than the end-to-end of the Billroth I procedure. I think it is preferable because it does not have the tendency to constriction at the site of anastomosis, and one is not limited by the diameter of the stump of the duodenum in the size of that anastomosis.

By having a larger anastomosis, one accomplishes two things: First, it removes the possibility of future obstruction or interference with proper emptying of the stomach; and secondly, by getting quite a wide anastomotic opening, one insures the rapid neutralization of such gastric acidity as is left by immediate mixing with the alkaline duodenal contents. This we feel can be better accomplished by putting the cut end of the stomach into the side of the duodenum where one is not limited in any way by the diameter of the duodenum.

As for the type of gastrostomy which Doctor Horsley has described, I have had no experience whatever. It does seem that it possibly offers a very useful adjunct at times when one has a patient where it is reasonable to suppose he or she will not tolerate the use of a nasal tube postoperatively.

DR. FRANK H. LAHEY (Boston): While this ulcer problem has been quite well threshed over, we all ought to relate our experiences with it because it is still an unsettled one. It is very evident that operative procedures for ulcer are by no means standardized. First of all, I do not think that 80 per cent of these patients get well with medical treatment.

I dislike to speak of figures, but they must be mentioned. We have now had 3,500 patients with ulcers in bed under bad management. Only 8 per cent of the patients with duodenal ulcer have been operated upon, and only 23 per cent of those with gastric ulcer, but all the others are not well. On the other hand, they are not sufficiently ill so that they need to have an operation and subtotal gastrectomy.

As to the problem of surgical management, I disagree definitely with any procedure which may incline one to make anything but radical removals of large portions of the stomach in patients who have had repeated hemorrhages or who possess the other features of failure under medical measures. Any procedure, such as the Billroth I operation, that attempts to attach a short stump of the stomach to the fixed duodenum will very definitely incline one to make inadequate gastric resections. We are, therefore, not interested in any type of procedure of dumping gastric contents into the duodenum at the expense of radical removal of large parts of the stomach.

There are one or two other points, based upon our experience representing now something over 200 subtotal gastrectomies for ulcer. An important point, I think, in the management of duodenal ulcers is first to settle the relation of the ulcer to the common bile duct. I know nothing that has been more distressing to me than to resect the portion of the duodenum containing the ulcer and then find I did not have enough duodenum left to satisfactorily and safely close it.

The other point that I wish to make is that we now have performed the Finsterer resection by exclusion operation in 20 cases. This consists of leaving the ulcer when it is not one in which recent hemorrhage has occurred, turning the end of the stomach in proximal to the pylorus, then performing a high gastric resection. The end-results of these followed cases have been just as satisfactory as have been the cases in which subtotal gastrectomy together with removal of the ulcer-bearing duodenum has been performed.

One other fact is that when you attempt to perform subtotal gastrectomy with clamps, you will be limited in the height of the resection. When you undertake them without clamps, you can resect them as high as you want to.

DR. ROSCOE R. GRAHAM (Toronto, Canada): I should like to ask Doctor Horsley if he has had any pancreatic fistulae follow in these cases. We have had experiences that are at variance with his. In a group of cases, when a portion of pancreatic tissue was resected together with the ulcer, the convalescence was complicated too often by a pancreatitis, which in one instance proved fatal. In a second group of cases, when we have interfered with the pancreas when a penetrating posterior wall duodenal ulcer was present, and then restored the continuity of the gastro-intestinal tract by an end-to-end anastomosis of stomach to duodenum, we had, in two such cases, within three months, a recurrence of ulcer at the line of anastomosis. We, therefore, now never establish continuity of the gastro-intestinal tract following an operation for duodenal ulcer unless we have been able to remove all evidence of local pathology. In view of the fact that we believe surgical procedures, and particularly gastrectomy, are contraindicated except in complicated duodenal ulcers, it becomes obvious that it is rarely possible to carry out this procedure.

With adequate preoperative preparation by means of an indwelling duodenal tube over a period ranging from two to three weeks, we believe that the



risk of opening the proximal gastro-intestinal tract is not great. This is based upon the fact that repeated lavage decreases the associated periduodenal edema which involves not only the pancreas, but other periduodenal tissues. With this belief, we pinch off the duodenum from the ulcer base, which is left *in situ* on the pancreas, and is exteriorized by closing the duodenum and then turning the closed end into the ulcer base, where it is held by interrupted silk sutures. This, in our hands, has obviated the postoperative complications of pancreatitis.

I should like again to emphasize the point which Doctor Lahey has made, that there very rarely is any indication for an operation for duodenal ulcer which is combined with restoration of the gastro-intestinal tract in continuity, not for the reason which he stated, that it is impossible to perform a sufficiently adequate resection, as we believe this is possible, and we practice it in the gastric ulcers, but because in our experience the incidence of recurring ulcer at the site of the anastomosis is high. We are convinced in such cases that a radical subtotal gastrectomy, with removal of the entire lesser curvature, which is readily accomplished with the use of a Schoemaker clamp, offers the greatest safeguard for the patient's future.

DR. J. SHELTON HORSLEY (closing): Some of the objections made have been dealt with in the paper. It was too long to read all of it.

In regard to Doctor Finney's preference for the end-to-end method, I will say that in perforating duodenal ulcers it is necessary to close the stump if an end-to-side of the stomach to the duodenum is done. If there is a duodenal perforating ulcer shaved from the pancreas, the stump of the duodenum is very short and the closure of the stump of the duodenum to make an end-to-side union is somewhat of a problem. If the duodenum is flared open by an incision as shown in the illustration, there is very little danger of constriction, and the duodenum can be sutured to the stomach after bringing the posterior wall of the stomach, covered with peritoneum, over to the short stump of the duodenum and tucking it in. If the suture does happen to leak, there is a posterior solid wall of pancreatic tissue, made sterile by the cautery.

If there is a recurrent ulcer—in two of these cases I have had to do this—a posterior gastro-enterostomy is a much simpler procedure than performing a posterior gastro-enterostomy first, having a recurrent ulcer, and then disconnecting it and performing a partial gastrectomy.

As to the union of the stump of the stomach to the jejunum, in many of these cases there is a tendency to recurrence, and the farther down in the intestinal tract, the more sensitive is the mucosa to the acid of the stomach. Particularly in the type of case that suffers a great deal of discomfort, it seems to be much better to do what might be called a physiologic method by uniting the stump of the stomach to the stump of the duodenum along the lesser curvature and if there is a recurrence, it can be treated more simply later on by gastro-enterostomy.

As to the question of Doctor Graham, I have never had a pancreatic fistula in any of these cases. Remember that this is shaving off a very thin slice of adherent pancreas with the hot cautery. As to leaving the ulcer and performing a partial gastrectomy by the Finsterer method, of course many of these patients get well, but, after all, in the long run it seems better to follow physiologic lines and remove the infected ulcer than to leave it and unite the stomach to the jejunum.

If you leave a focus of infection, which the perforating ulcer is, you also leave a pancreatitis, which may extend and later the patient may be affected by this septic focus that you purposely left behind.

## LATERAL GASTRODUODENOSTOMY IN CERTAIN CASES OF DUODENAL AND RECURRING ULCER\*

VERNE C. HUNT, M.D.

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GRAHAM, among others, has directed attention to the many factors which require due consideration in the selection of the surgical procedure for ulcer which may be best suited in the individual instance. He said: "The patient who accepts operation expects recovery from the operation, relief from the symptoms, security against recurrence, and restored economic efficiency. In order to achieve this desired result, the surgeon in determining the correct operative procedure must take into consideration the site of the ulcer, the character of the lesion, the associated physiologic disturbances, the result of the biochemical disturbances, and the age of the patient."

The variety of operative procedures which may be instituted in the surgical treatment of ulcer provides opportunity to achieve the desired result in a high percentage of instances, but for these results to be achieved requires versatility on the part of the surgeon. While a particular procedure may be executed upon many patients with ulcer, in whom the various factors approximate similarity, dissimilarity occurs so frequently that one must be prepared to select and execute that operation which most nearly accomplishes the purpose of surgical treatment in the particular instance.

It is not my intention at this time to discuss the relative merits of the various operations for duodenal and recurrent postoperative ulcers; suffice it to reiterate that no single operation is applicable in all instances of either type of ulcer. Broadly considered, the medical and surgical treatment of ulcer is directed toward control of gastric acidity and gastric secretion. Surgically, this may be accomplished either through neutralization and dilution by conservative operations, or through quantitative reduction of gastric acidity by partial gastrectomy. Even from a conservative viewpoint, a radical, partial gastrectomy may be and often is the operation of choice in certain cases of duodenal ulcer, particularly in those from which one or more massive hemorrhages have occurred, and in many cases of postoperative recurrent ulcer. Also, from a less conservative viewpoint, the magnitude of a partial gastrectomy may be, and not infrequently is, too great under certain circumstances when an opportunity is provided for the selection of a less drastic surgical procedure which may still accomplish the purpose of an operation with a minimum risk. The object of this discussion is to again direct attention to the merits of an operation which seems to justify its employment more often than it has been employed in the past.

The operation of lateral gastroduodenostomy is not new in principle, but

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\* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

certain important details of recent contribution aid materially in the execution of the operation and enhance the immediate and late result. In 1892, Jaboulay suggested, and, in 1894, first performed a gastroduodenostomy as an anastomosis between the upper portion of the second or descending portion of the duodenum with the anterior wall of the stomach. The duodenum was not mobilized, but the stomach was drawn over and sutured to it. Experiences with the operation of gastroduodenostomy have been reported by Kocher, Moynihan, Balfour, Wilkie, Reinhoff, Clute and others. J. M. T. Finney, Sr., was perhaps the first to mobilize the entire first part and upper half of the second portion of the duodenum. It is of interest that as he, the originator of the Finney pyloroplasty, and J. M. T. Finney, Jr., have had an increasing experience with the operation of pyloroplasty, they have extended the incisions in both the stomach and the duodenum, thus providing a large stoma between the stomach and duodenum. In so doing, they have made duodenal content of a maximal degree of alkalinity available for neutralization or dilution of gastric content, at a level from which reflux of duodenal content into the stomach can readily occur. In other words, the operation of pyloroplasty has been extended to embrace the advantages of lateral gastroduodenostomy. Because the scope of the operation has been enlarged to include more of the stomach and the duodenum than the original procedure, it may hardly be considered a true pyloroplasty, and is best designated by the recently applied term, gastropyloroduodenostomy.

*Physiologic Principles.*—Many observers agree that the reduction of gastric acidity, when it occurs following the conservative operations for duodenal ulcer, is due chiefly to an admixture of duodenal content with that of the stomach, and that perhaps most of the reduction of gastric acidity occurs through dilution instead of neutralization. In my own experience, the various types of pyloroplasty or operations confined to the pylorus, first portion of the duodenum and the prepyloric portion of the stomach, have been followed by results incomparable to those following practically all other types of operation instituted in the treatment of duodenal ulcer, and as a consequence have been abandoned. Most of the unsatisfactory results which follow operations upon the pylorus, embracing division of or excision of a major portion of the pyloric muscle, with or without excision of the duodenal ulcer, have been due either to reactivation of a persisting ulcer in the posterior wall of the duodenum or to recurrence of an ulcer in the suture line of the pyloroplasty. In retrospect, this is as might be expected. The alkalinity of the duodenal content in the suprapapillary and in the subpapillary portions of the duodenum is not equal nor of the same degree. There is also considerable evidence which tends to support the idea that the reaction of the duodenal content in the first portion of the duodenum, particularly in patients who harbor an ulcer, is on the acid side rather than on the alkaline side. Furthermore, that actual regurgitation of duodenal contents through a permanently abolished pyloric muscle in amounts sufficient to provide much diluent or neutralizing

effect, or that regurgitation occurs at all, have not been firmly established. The sum total of gastro-intestinal motility is downward and not upward. Considerable evidence is at hand to indicate that marked reduction in gastric acidity results when an admixture of duodenal and gastric contents occurs through a downstream by-pass and that little if any reduction results when such an admixture is dependent upon upstream regurgitation. Hill, Henrich and Wilhelmj, in a study of the changes in the gastric acidity in the experimental animal produced by various operations on the stomach, stated that after a Heineke-Mikulicz type of pyloroplasty the acid curve is almost the same as that in a normal dog; that after gastrojejunostomy the reduction in acidity is striking; and that after gastroduodenostomy the reduction is even more marked. Fundamentally, it would seem that the various operations designated as pyloroplasty fail to embrace the important principle in the surgical treatment of duodenal ulcer; namely, the control of gastric acidity and gastric secretion either through dilution and neutralization or through quantitative reduction.

Posterior gastro-enterostomy has been, and still remains, an operation of choice in many cases of duodenal ulcer, and when accurately executed in carefully selected cases it is followed by excellent results. Only one disconcerting factor—marginal or jejunal ulcer of variable incidence—limits its general usefulness. It is well known that the intestinal mucosa possesses or lacks (depending upon the segment) resistance to ulceration, and that perhaps the maximum degree of resistance exists in the second and third anatomic portions of the duodenum. Whether or not this is due to true inherent resistance in the mucosa or whether it is the result of the protection afforded the mucosa in these sections by the alkaline bile and pancreatic secretions remains a question. Without here presenting the evidence, the latter seems more probable. At any rate, it is now recognized that the degree of alkalinity of the duodenum is highest at the level and immediately below the papilla of Vater, as the result of the outpouring into the duodenum of bile and pancreatic secretion. While marginal, gastrojejunal or jejunal ulcer occurs with a variable frequency following posterior gastro-enterostomy, ulceration in or about the stoma of a lateral gastroduodenostomy seldom if ever occurs. Finney has said that an anastomotic ulcer does not follow; Flint, in his wide experience with the operation, has not seen an ulcer in the stoma of a gastroduodenostomy; Wilkie had two cases of stomal ulcer in his experience. In view of the physiologic processes concerned, lateral gastroduodenostomy should provide greater assurance against the development of an anastomotic ulcer than any other type of gastro-intestinal anastomosis excepting the Haberer end-to-side gastroduodenal anastomosis. It seems most probable that the greatest degree of dilution and neutralization of gastric acidity by duodenal contents is possible through a stoma at or just below the duodenal source of the diluent and neutralizing agents, bile and pancreatic secretions. Furthermore, it seems entirely logical that the mixing of duodenal contents of a maximum degree of alkalinity with gastric secretions at this level provides dilution and neutrali-

## LATERAL GASTRODUODENOSTOMY

zation at the proper time and place to be most effective. The experimental work of Graves and that of McCann suggests at least that the effectiveness of duodenal alkaline secretion upon gastric acidity is greater when it is emptied into the stomach downstream or into the prepyloric area than when it is diverted upstream into the fundus of the stomach.

*Applicability of Lateral Gastroduodenostomy.*—Certain limitations in the applicability of lateral gastroduodenostomy exist and for the most part these are dependent upon anatomic relations and the mobilization of the duodenum. There are no true anatomic barriers to free mobilization of the third and



FIG. 1.—The filmy reflection of the peritoneum is divided lateral to the duodenum, which allows elevation of the duodenum from its retroperitoneal position.

fourth portions of the duodenum except the superior mesenteric artery and vein which can be accurately visualized and preserved. In 1932, Reinhoff described an infrapapillary gastroduodenostomy and stated that he had successfully operated upon 13 cases of chronic peptic ulcer by this method, with excellent results. His procedure facilitates anastomosis of the third portion of the duodenum with the antrum of the stomach through mobilization of the entire duodenum, including its fourth portion to and beyond the ligament of Treitz. In my own experience, such extensive mobilization has not been necessary. The filmy reflection of peritoneum overlying the duodenum is readily divided, thus facilitating the elevation of the duodenum from its retroperitoneal position for a liberal anastomosis without angulation (Fig. 1).



Clute and Sprague have recently illustrated methods by which angulation may be avoided.

During the past few years lateral gastroduodenostomy has been employed in 22 cases, with no deaths and but few instances of temporary gastric retention, and has been followed by excellent results. In 13 cases, the operation was readily applicable as a primary operation of choice for duodenal ulcer in which either posterior gastro-enterostomy or partial gastrectomy could have been performed. In nine cases, a previous gastro-enterostomy had been fol-



FIG. 2.—Mobilization of the duodenum facilitates its approximation to the antrum of the stomach without angulation or undue tension.

lowed by marginal or jejunal ulcer and instead of performing a partial gastrectomy the gastrojejunal anastomosis was taken down, the marginal or jejunal ulcer was excised and a lateral gastroduodenostomy was employed. A gastrojejunal fistula existed in two cases. The satisfactory results which followed in these cases justify conservative surgical procedures in many cases in preference to radical partial gastrectomy. Snell has directed attention to the element of mechanical difficulty as the result of deformity of the pyloric outlet produced by the operation of lateral gastroduodenostomy. Judging from my experience, the amount of such deformity is dependent upon how thoroughly the duodenum is mobilized. Worthy of emphasis is the fact that

## LATERAL GASTRODUODENOSTOMY

in performing a lateral gastroduodenostomy it is necessary that the duodenum be carried over to the stomach instead of the stomach being drawn over to the duodenum (Figs. 2 and 3). The operation is not applicable in all cases, by virtue of anatomic relationship variations, and should not be forced when deformity of the pyloric outlet or angulation of the duodenum below the anastomosis is likely to result.



FIG. 3.—The anastomosis is made without clamps on either the stomach or the duodenum.

To those surgeons who have abandoned gastro-enterostomy for duodenal ulcer or who employ the procedure with misgiving on account of the variable frequency with which in their experience marginal ulcer either as true gastro-jejunal or jejunal ulcer has occurred, lateral, subpyloric gastroduodenostomy in certain cases should appeal. To those who are not wholeheartedly committed to the theory and principle of partial gastrectomy for duodenal ulcer, the operation of gastroduodenostomy provides a conservative surgical procedure which at times may be employed with maximum assurance against recurrence or new ulcer formation at or about the stoma. Likewise, the operation serves admirably as a secondary procedure in certain cases when an operation is necessary subsequent to a simple closure following an acute per-

foration, or in occasional instances of recurrent ulcer subsequent to pyloroplasty or gastro-enterostomy.

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## EXPERIMENTAL PROOF OF THE OBSTRUCTIVE ORIGIN OF APPENDICITIS IN MAN\*†

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In a preliminary study,<sup>10</sup> reported two years ago, from observations made upon the exteriorized, unobstructed appendix, evidence was presented which suggested that the vermiform appendix of man secreted fluid. It was also shown, at that time, that obstruction of the cecal appendage of the rabbit was followed consistently by evidence of rapid fluid secretion. During the time that has intervened since then, these studies have been extended considerably. In the present communication evidence of the secretory capacity of the vermiform appendix of man will be cited.

The behavior of the appendix when obstructed temporarily will be described and factual proof of the reproduction of the pathologic picture of spontaneous appendicitis through the agency of obstruction will be presented.

*Method.*—From studies made upon the obstructed cecal appendage of the rabbit and the vermiform appendix of the chimpanzee,<sup>11</sup> it was apparent that in order to adduce convincing proof of the secretory capacity of the appendix of man it was necessary to incannulate the obstructed exteriorized appendix. Unobstructed appendicostomies permitting incannulation had been established incidentally when colostomy was performed for malignant disease of the colon. Exteriorization of the appendix in this manner had been accomplished readily through a button-hole incision and did not complicate the operative procedure.<sup>10</sup>

In a patient presenting a carcinoma of the ascending colon, it was possible to exteriorize, with the blood supply intact, after the Bloch-Mikulicz principle, the greater portion of the right half of the colon and the terminal ileum. A few days later, when the exteriorized bowel had become fairly well covered with fibrin and effectual sealing of the wound had occurred, the base of the appendix was ligated securely. The attachment of a closed water system connected to a recording manometer permitted determination of the ensuing increase in intraluminal pressure. The manometer used required addition of 0.58 cc. of fluid to raise the pressure reading 100 cm. of water.

It was obvious that this type of case, permitting determination of the secretory capacity of the vermiform appendix, would not be encountered frequently. After considerable deliberation the method depicted in Figure I was worked out. When preliminary colostomy was being performed for malignancy of the large bowel or rectum prior to excision of the lesion, the appendix

\* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

† The researches presented herewith were supported by a grant of the Graduate School of the University of Minnesota, and also by a grant for technical assistance by the Federal Public Works Administration, Project No. 665-71-3-69, Subproject No. 258.

was exteriorized and obstructed. Through a button-hole incision placed over the base of the cecum, the appendix was delivered and the cecum around the base of the appendix was anchored securely to the parietal peritoneum by a number of fine silk sutures, thus placing the appendix in an extraperitoneal position. The base of the appendix was ligated with plain catgut No. 00, a cannula was placed in the appendix and as soon as the patient was returned to his room attachment was made to a manometric recording system. After it was determined whether or not the obstructed exteriorized appendix developed an increase of intraluminal pressure, the closed system was broken and the cannula was attached to a small Wassermann tube (atmospheric pressure)

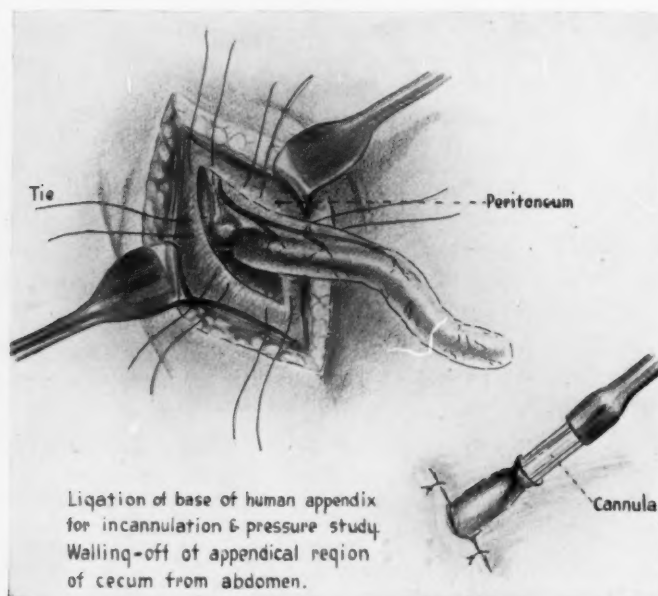


FIG. 1.—Technic of exteriorizing and obstructing an appendix as employed in this study for purposes of measuring the secretory pressure—a procedure performed coincidentally at the time of colostomy.

to note whether fluid could be collected. At this juncture a segment of the distal portion of the appendix was excised for purposes of histologic comparison with the segment removed as a control section at the time of operation. In a few instances leukocyte counts were made to determine whether increases of intraluminal pressure caused leukocytosis. No appendix was allowed to go on to perforation.

Before dismissal of the patient from the hospital, the appendix was snipped off at the level of the skin and granulations grew over its orifice and skin soon covered the site where the appendix had been eviscerated.

In a few instances in which the appendiceal stump continued to secrete fluid, extraperitoneal excision of the residual segment beneath skin level was made.\*

\* No patient in the series came to harm through any of these manipulative procedures incidental to exteriorization of the appendix.



*Results.*—The secretory activity of the obstructed appendicostomies is summarized in Table I. The cases have been grouped in the table with reference to the heights of secretory pressure attained. It is to be noted that the highest recorded pressure was 126 cm. of water, a level reached 22 hours after exteriorization and obstruction of the appendix in a man age 68. The next highest pressure recorded was 125 cm. of water, reached after 14 hours and 15 minutes in a man age 47. In a man, age 70, pressure of 92 cm. of water was reached 14 hours and 30 minutes after incannulation. The oldest patient in the series was age 75 (Case 20). No evidence of fluid secretion was noted. The appendix had a lumen but microscopic examination showed no evidence of mucosa. One patient in the series, R. A., Case 7 in the table, was age 29;



A

FIG. 2.—A. The patient and the manometric recording system for determining secretory pressure (Case 1, Table I).

G. L., Case 3, was age 33; the next youngest patient in the entire group was age 41. The average age for the group was 56.

No secretory pressure developed in three of the 22 exteriorized, obstructed appendixes. One of these was M. F., Case 20, age 75, referred to immediately above. In another, Case 22, G. B., age 53, whose cecum was exteriorized for polyposis, the blood supply of the appendix had been damaged in the manipulative maneuvers necessary to exteriorize the cecum and appendix and the negative result is essentially without significance. In the instance of a third patient, Case 21, A. C., age 61, the cannula had not entered the lumen and no secretory pressure was recorded. When the appendix was removed, however, exudate was found in the lumen.

In six other instances, however, a secretory pressure of less than 20 cm.

TABLE I  
STUDIES OF SECRETORY CAPACITY OF OBSTRUCTED, EXTERIORIZED APPENDICES IN MAN

Case No.	Initials, Univ. Hosp. No. Sex and Age	Maximum Pressure (Cm. Water)	Duration		Total Fluid After End of Recording (Cc.)	Period of Fluid Collection (Days)	Lapse of Time Between Onset of Experiment and Removal of Appendix	Histologic Study	
			Time Required to Reach Maximum Pressure (Hrs.)	Pressure Sustained (Hrs.)				Control Section	After Pressure
(1)	T.W. No. 665959 M. 68	126	22	2 3/4	3.5	2	25 hrs.	Good mucosa	A.D.A.*
(2)	O.N. No. 662989 M. 47	125	14 1/4	1/2	12.5	6	3 days	Good mucosa	A.D.A. with necrosis
(3)	G.L. No. 660228 F. 33	114	35	14	3.25	5	50 hrs.	Good mucosa	A.D.A.
(4)	P.G. No. 661973 M. 70	92	14 1/2	7 1/2	1.5	2	48 hrs.	Good mucosa	A.D.A.
(5)	C.P. No. 663022 M. 56	90	16 1/2	3	0.5	1	20 hrs.	Good mucosa	A.D.A. Loss of mucosa with fragmentation of muscle
(6)	U.T. No. 666978 M. 53	86	25 1/2	0	?		Not removed	Good mucosa	No sections
(7)	R.A. No. 661380 M. 29	85	27	0	7.0	7	Not removed†	Good mucosa	No sections
(8)	M.K. No. 667935 M. 54	60	3 1/4	5 1/2	0.5	2	Not removed†	Good mucosa	Mild A.D.A. with exudate in lumen
(9)	W.P. No. 660521 M. 45	42	12	9	0	0	21 hrs.	No sections	
(10)	F.H. No. 661415 F. 60	32	7	0	5.5	5	2 mos.	No sections	
(11)	P.S. No. 664561 M. 73	24	24	0	0	—	Not removed†	Atrophic mucosa at distal end	
(12)	W.H. No. 671573 M. 53	20	(See text—pressure not allowed to rise above 20 cm.)				Not removed	Good mucosa	
(13)	T.C. No. 666127 M. 66	20	24	0	0	2	Not removed	Much fat in sub-mucosa	

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(14) A.O. No. 665635 F. 53	17	20	0	7.2	8	Not removed	Fair mucosa with much lymphoid tissue	No sections
(15) E.B. No. 665350 M. 58	15	18	0	0	—	Not removed†	Atrophic mucosa with much fat	No sections
(16) W.B. No. 665646 M. 67	11	17	0	0	—	Not removed†	Atrophic mucosa with much fat	No sections
(17) A.B. No. 664251 F. 41	8	2	24	7.4	13	13 days	No mucosa in control	Serositis; few leukocytes in muscle layer
(18) J.S. No. 667657 M. 57	6	25	0	0	—	Not removed	No mucosa in control	No sections
(19) A.T. No. 662354 M. 62	5	1	18	1.1	4	Not removed†	No mucosa in control	No sections
(20) M.F. No. 663863 M. 75‡	0	—	—	0	—	26 hrs.	No mucosa in control	Mucus with leukocytes in lumen
(21) A.C. No. 653835 F. 61‡	0	—	6 days	0	—	6 days	No sections	No sections
(22) G.B. No. 661495 M. 53§	0	—	—	1.0	2	6 days	No sections	No sections

\* A.D.A. abbreviation for acute diffuse appendicitis.

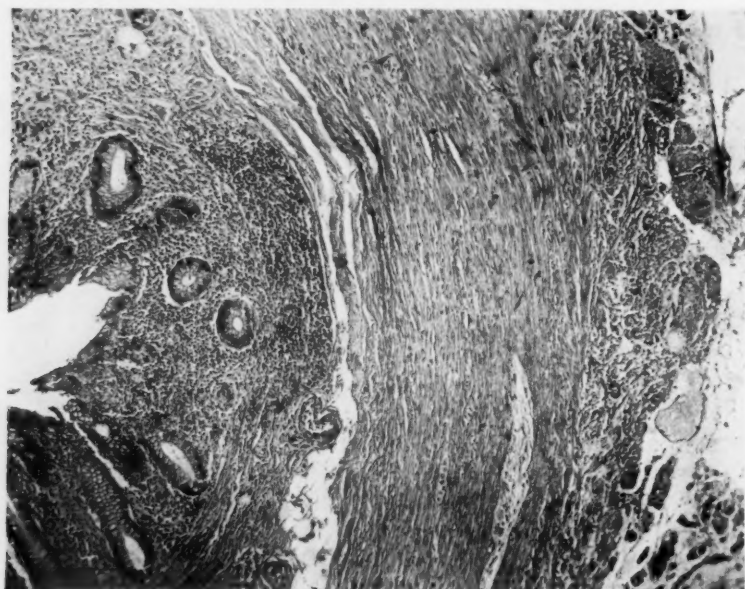
† Too short for removal.

‡ Short mesentery; appendix under tension when exteriorized.

§ Appendix devascularized during exteriorization.

of water was recorded. In one of these, Case 17, A. B., age 41, the appendix had no mucosa. In the five others (Cases 14, 15, 16, 18 and 19), the segment of obstructed, exteriorized appendix was so short that on removal of the cannula, no specimen could be removed for biopsy.

In nine instances, the highest secretory pressure exceeded 40 cm. of water; in seven of these the pressure was sustained above 85 cm. In four instances, pressures intermediate between 20 and 40 cm. of water attended obstruction of the exteriorized appendix. In one of these, Case 12, W. H., age 53, the pressure was not allowed to mount over 20 cm. of water. As soon as that level of pressure was reached, the recording lever was lowered to zero by re-

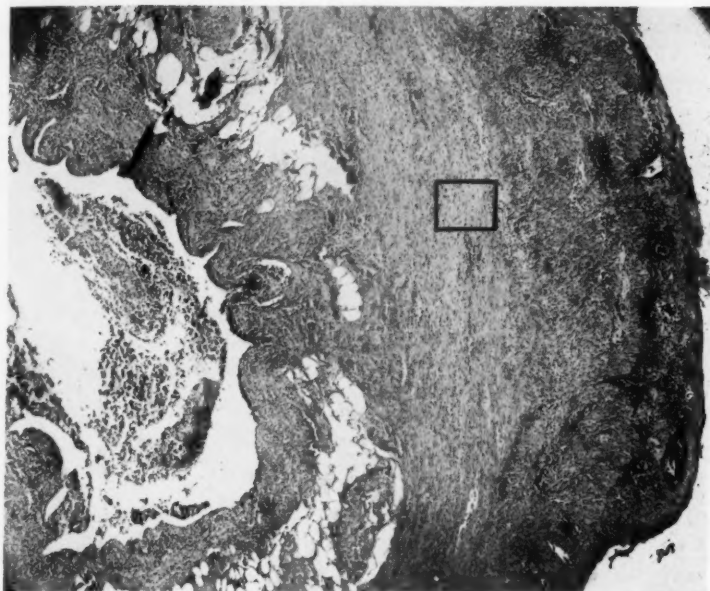


B

FIG. 2.—B. The control section—cut from the distal end of the appendix at the time the exteriorization was performed. ( $\times 60$ )

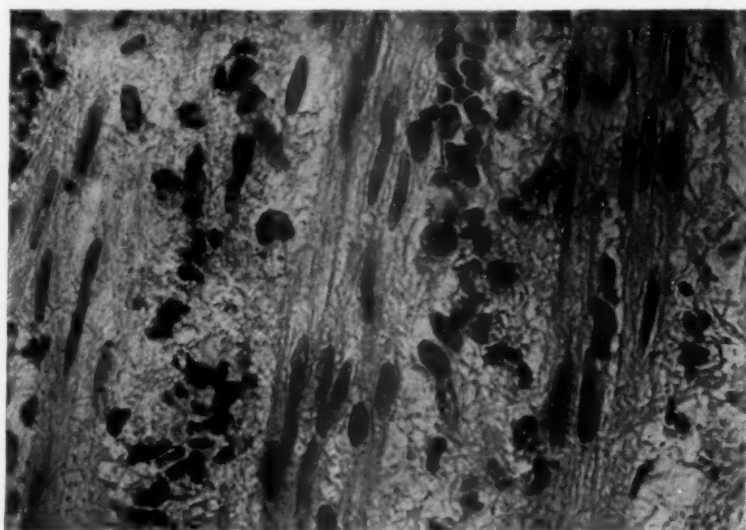
moval of fluid from the system by an aspirating syringe. On the first occasion, it took but 30 minutes for the level of 20 cm. of water pressure to be developed. After a wait of 20 minutes, it took 50 minutes to develop the same level of secretory pressure. After an interval of 24 hours, the level of 20 cm. pressure was reached in 18 minutes; on the third day it took 80 minutes and the same amount of time on the fourth day.

*Discussion.*—These data support the thesis that the vermiform appendix of man, when obstructed, will develop a secretory pressure in the majority of instances which will threaten the viability of the appendiceal wall. It is to be noted, however, that there are instances in which no evidence of secretory pressure attends luminal obstruction. Such appendices undoubtedly would tolerate luminal obstruction without hazard to their owners. The instance of W. H., Case 12, suggests that luminal obstructions which are survived di-



C

FIG. 2.—C. After 25 hours of pressure. ( $\times 30$ ) The square indicates the site from which D was taken. There is a diffuse cellular infiltrate with exudate in the lumen. The fat in the submucosa is also apparent.



D

FIG. 2.—D. A free exudation of polymorphonuclear cells has occurred into the muscular layer. ( $\times 500$ ) (The print has been turned to include visualization of a greater length of the muscle layer.)



minish the secretory capacity of the appendix. It is apparent, not alone from the small amount of fluid secreted by the normal appendix but by instances in which no evidence of fluid secretion was obtained, as well by the observations made on W. H., Case 12, cited above, that the balance between secretion and absorption, though weighted in the favor of the former, is poised on a somewhat narrow margin.

In the main, a fairly definite correlation was found to exist between normal microscopic appearance of the mucosa in the control section and the development of a high secretory pressure. This factor would appear to be the most significant item in determining whether an obstructed appendix will secrete fluid. Obliteration or connective tissue replacement of the luminal mucosa is certain to be correlated with a lack of secretory capacity in the vermiform appendix. The presence of fat in the submucosa, if the mucosa itself is normal, does not militate against the development of high secretory activity (Fig. 2C). An abundant lymphoid tissue, beneath an atrophic mucosal layer, does not assure rapid fluid production (A. O., Case 14, Table I).

*Appendicostomy—with base tied  
Closed System  
Case of T. W.  
(Case I, Table I)*

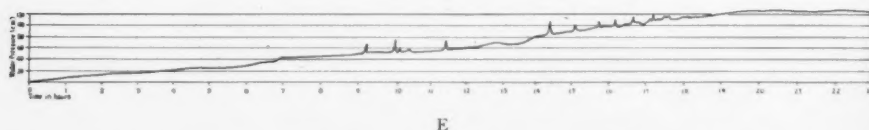


FIG. 2.—E. Retraced pressure record—the slope of the rising pressure is indicated. A pressure of 126 cm. water was reached 22 hours after obstruction.

It would appear, therefore, that the more normal the appendix, the more likely it is when obstructed to secrete fluid rapidly, pyramiding the intraluminal pressure with resultant anoxic effects upon the appendiceal wall. The disintegration of the wall of the appendix eventuating in perforation or gangrene is owing in part to the fluid transudation occasioned by the resistance of the high intraluminal tension and in part by cellular migrations into the wall as well as through bacterial invasion. A normal appendix which will withstand an intraluminal tension of approximately three atmospheres of pressure without rupturing, immediately after excision will perforate at very low values (20 to 70 cm. of water pressure) if it had been subjected to prolonged maintenance of sustained intraluminal pressures within the range of secretory pressures recorded in Table I. It is to be recalled that the luminal capacity of the normal appendix at atmospheric pressure is essentially zero, and that at 60 cm. of water pressure the usual luminal volume of the normal appendix is about 0.5 cc.<sup>10</sup>

Whereas, in an earlier study,<sup>10</sup> the impression was lent on the basis of a study of the secretory behavior of the cecal appendage of the rabbit that catharsis accelerated fluid secretion, a more adequately detailed controlled study of this item suggests that neither fluid secretion nor perforation is hurried by purgation.<sup>4</sup> In the rabbit, obstruction of the cecal appendage will be followed

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by perforation in 75 per cent of instances within 10 hours after ligation of the base. The administration of cathartics induces movements of the appendix

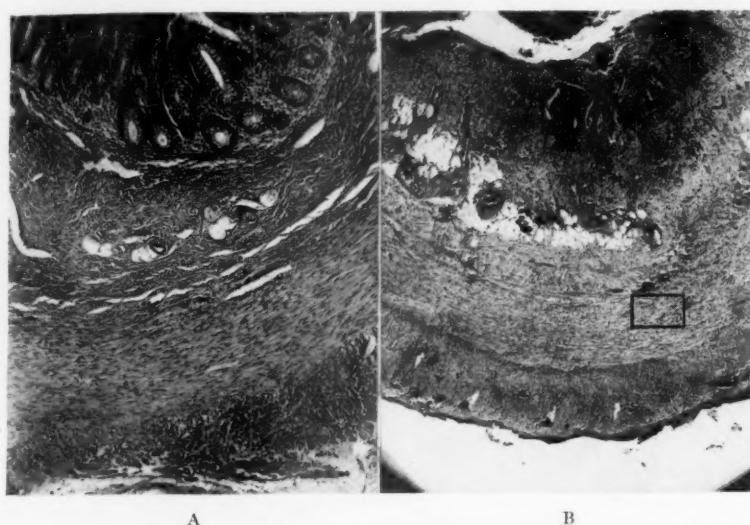


FIG. 3.—Photomicrographs of Case 3, Table I. A pressure of 114 cm. of water was reached after 35 hours. (A) The control section removed at the time of obstruction and exteriorization of the appendix. ( $\times 65$ ) (B) After 50 hours of sustained pressure. There is a diffuse cellular reaction throughout the wall—some exudate is present in the lumen ( $\times 65$ ).

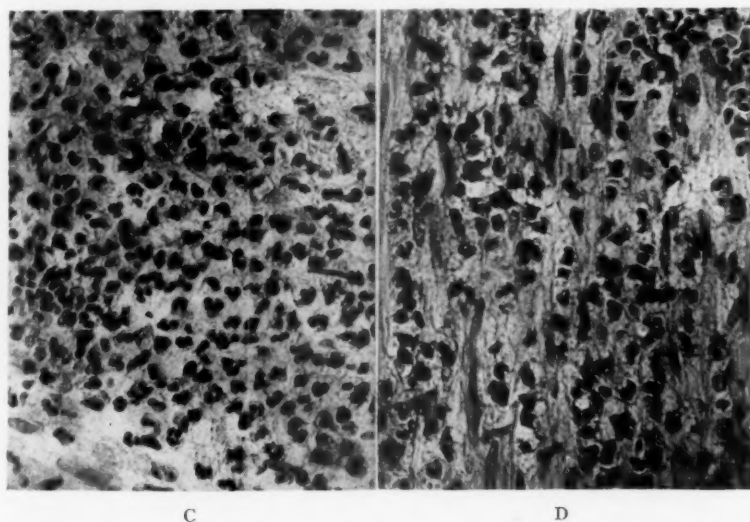


FIG. 3.—(C) Higher magnification of the submucosa as shown in B. ( $\times 550$ ) The exudation of polymorphonuclear cells into the submucosa is apparent. A few muscle cells may be seen in the lower portion of the section. (D) Higher magnification from lower square as shown in D. ( $\times 550$ ) The section is turned on the side to permit inclusion of a greater portion of the muscle layer. Many polymorphonuclear cells may be seen scattered among the spindle-shaped muscle nuclei.

which preclude effectual sealing-off at the site of perforation by adjacent coils of intestine or other peritoneal surface.<sup>4</sup>

*Histologic Study of Obstructed Appendixes.*—It is to be conceded freely, that the vermiform appendix exteriorized upon the abdominal wall is not a properly controlled experiment for histologic observations. Every appendix exteriorized in this manner, whether or not it develops a high secretory pressure, exhibits evidence of thickening of the peritoneal tunic of the appendix (serositis). In two unobstructed, exteriorized appendixes, employed for purposes of control in which a catheter was left in the lumen, in one instance (case of C. S., age 65, U. H. No. 670933) for six weeks before excision of the specimen and in the other 12 days (case of B. N., age 33, U. H. No.



FIG. 4.—Section of a gibbon's obstructed appendix after 22 hours of incannulation. The highest pressure reached was 19 cm. of water—a pressure sustained for less than one hour. There is evidence of serositis. Otherwise the section is normal.

660885), the lumen and mucosa in each instance were normal. Both exhibited marked serosal thickening and cellular infiltration was apparent in the muscle layer.

Our best controlled observations were upon the obstructed appendixes<sup>11</sup> of apes. Here, it was possible to leave the obstructed appendix within the peritoneal cavity or at least well beneath the skin. In the chimpanzee, which develops with luminal obstruction a secretory pressure not unlike man or the rabbit, a diffuse cellular infiltration of all the walls attends obstruction. In

the gibbon, on the contrary, in which the highest pressure attained was 20 cm., and not long sustained, luminal obstruction was not attended by leukocytic invasion of the walls (Fig. 4). A mild serositis only attended the exteriorization.

As has already been related in the statement concerning the results of luminal obstruction of the vermiform appendix of man, the best determinant of whether an appendix will secrete fluid and develop the histologic picture of acute diffuse appendicitis consequent upon obstruction, is the presence of a normal mucosa. All instances in which high secretory pressures followed obstruction were attended by the histologic pictures of acute diffuse appendicitis. The histologic study of two of these (Cases 1 and 3, Table I) is shown in Figures 2 and 3. The details of the histologic findings are listed in Table I.

Dr. R. E. Buirge,<sup>3</sup> of this Clinic, has made cell counts of the exudate found within the lumen of appendixes exhibiting no demonstrable evidence of inflammation within its wall as well as upon the exudate within the lumina of appendixes exhibiting definite evidence of acute diffuse appendicitis. Similarly, he has made cell counts upon the exudate appearing in the lumina in a number of the patients in this series whose appendixes were obstructed and exteriorized. It is well known that cells are extruded constantly into the intestinal canal and the exfoliation of epithelial cells from the appendiceal mucosa as well as extrusion of white blood cells through the intact appendiceal mucosa is generally accepted as a constantly occurring phenomenon.<sup>6, 7, 9</sup>

Buirge observed that this exudate, which may be observed not uncommonly within the lumen of an appendix, the wall of which fails to exhibit evidence of inflammation, possesses regularly a predominantly lymphocytic character.<sup>3</sup> In a group of seven such cases in the appendixes of man, out of 100 cells within the lumen the average lymphocytic count was 90. In instances of spontaneously occurring appendicitis, on the contrary, a count of the luminal exudate showed invariably a definitely predominant polymorphonuclear leukocytosis. In a group of 13 such instances, the average polymorphonuclear count on the luminal exudate was 86 cells out of every 100 counted. Similarly in a group of six obstructed, exteriorized appendixes in which fluid secretion was active, the cell counts on the luminal exudate showed the average polymorphonuclear count to be 82 cells out of every 100 cells counted. It is apparent, therefore, that the same type of cellular response attends obstruction of the exteriorized appendix as is observed in instances of spontaneous appendicitis. The exudation of polymorphonuclear cells into the muscle layer in obstructed exteriorized appendixes is apparent in Figures 2 and 3.

*Effect of Appendiceal Obstruction Upon Production of Pain, Fever and Leukocytosis.*—In a number of instances, careful notations were made with reference to pain or discomfort attending obstruction of the exteriorized appendix. The presence or absence of pain in these cases was difficult to determine in most cases or was rendered actually inconsequential by the administration of opiates to relieve postoperative pain. In the main, it would appear that a colicky pain not unlike that observed in spontaneously occurring appen-

dicitis could be reproduced by luminal obstruction in those patients whose appendixes secreted fluid actively and developed a high secretion pressure. In Case 5, Table I, the details of which are listed below, it is apparent that the pain could be reproduced almost at will by elevating or lowering the intraluminal tension within the appendix. It is obvious, however, after a fairly high intraluminal pressure has been sustained for some time, that the occurrence of pain may be modified in proportion to the degree with which the circular muscle of the appendix resists distention.

Both fever and a polymorphonuclear leukocytosis were fairly constant accompaniments of the intraluminal pressure which attended obstruction of the exteriorized appendix. It is difficult, of course, to evaluate with exactness the temperature and leukocyte response to the performance of the colostomy.

Determination of how the factors of pain production, fever\* and leukocytosis were influenced by obstruction of the appendix was made in a large number of the group. Observations noted at the time of the recording of the secretory pressures with reference to the occurrence of pain, fever and leukocytosis is indicated in a few of the actively secreting appendixes as listed below:

**Case 1, Table I.**—T. W., age 68. Obstruction and exteriorization of a rather long and free appendix. Insertion of cannula for recording pressure.

1 day prior to operation—W.B.C., 7,700; P.M.N., 62%.

At start of record—Temperature, 99.2° F.

After 4 hrs.—Temperature, 99.6° F.; pressure, 22 cm. water.

After 12 hrs.—Temperature, 99.8° F.; pressure, over 60 cm. water.

Waves occur with peaks every five to ten minutes (peaks up to 80 cm. water pressure).

After 14 hrs.—Pressure, 78 cm. water. Waves becoming smaller; W.B.C., 15,600; P.M.N., 82%.

16 hrs. after exteriorization—Pressure, 100 cm. water; temperature, 99.4° F. Appendix pale and distended, no serosal discharge; circulation present; no pain.

At 18 hrs.—Pressure, 115 cm. water. Waves smaller and peaks less high (up to 125 cm. water).

At 20 hrs.—Pressure, 125 cm. water; temperature, 100° F. Waves even smaller (see Fig. 2E).

At 22 hrs.—Pressure, 126 cm. water; W.B.C., 15,000; P.M.N., 89%.

Pressure recording stopped and pressure removed. The patient had denied pain earlier, but on removal of the pressure he stated that he was suddenly relieved of a dull aching pain in the right lower quadrant. This dull ache was not reproduced, however, by raising the pressure again.

38 hrs.—W.B.C., 13,000; P.M.N., 77%. There was a slight elevation of temperature for two days after release of pressure.

*Ultimate Outcome.*—Dismissed from hospital and returned later for posterior excision.

**Case 2, Table I.**—O. N., age 47. Obstruction and exteriorization of appendix followed by incannulation for recording pressure.

At 7 hrs. after start of record—Pressure, 80 cm. water with 4 cm. waves; temperature, 99.2° F.; W.B.C., 24,000; P.M.N., 86% (waves synchronous with pulse).

At 9 hrs.—Appendix looks tense. The larger vessels on the surface were engorged, but the areas between were blanched. Patient denied pain even to leading questions.

\* All temperature determinations are rectal.



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At 14 hrs.—Pressure, 125 cm. water with 2 cm. waves synchronous with pulse; W.B.C., 16,000; P.M.N., 86%. Appendix more blanched and there were fewer vessels holding blood. The volume of the appendix at this time was 1.25 cc. The temperature rose to a maximum of 101° F. at 21 hrs., then returned to normal in a few hours (Fig. 5).

*Ultimate Outcome.*—Carcinoma inoperable. Radon insertion.

Dismissed from hospital.

**Case 3, Table I.**—G. L., age 33. Obstruction and exteriorization of appendix followed by incannulation for recording pressure. Preliminary volume-elasticity determination showed a leak occurring between 80 and 120 cm. of water pressure (base not tied tight).

At 3 hrs.—Pressure, 22 cm. water; temperature, 99.6° F.

At 12 hrs.—Pressure rise ceased and pressure leveled off abruptly, presumably due to leakage into cecum or seepage; pressure 97 cm. water. Slight peristaltic waves every few minutes and also pulse waves.

At 15 hrs.—Pressure, 96 cm. water waves disappearing; temperature, 100° F.

At 18 hrs.—Pressure, 98 cm. water; W.B.C., 11,800. Patient has no complaints—occasionally questioning elicits confession of vague lower abdominal soreness "like a stomach ache."

At 19 hrs.—Pressure, 99 cm. water; temperature, 99.6° F. Pulse waves rise 1 to 1½ cm.

At 20 hrs.—Pressure, 101 cm. water. There are occasional peaks to about 120 cm. due to movements of the patient and followed by a gradual fall to a lower level as if some fluid had been lost.

At 23 hrs.—Pressure, 95 cm. water; temperature, 100.2° F.

At 26 hrs.—Pressure, 102 cm. water; W.B.C., 9,800; P.M.N., 89%.

At 27 hrs.—Pressure, 104 cm. water; temperature, 100.4° F.

At 28 hrs.—Pressure, 110 cm. water.

At 29 hrs.—Pressure, 106 cm. water. Lower abdominal discomfort.

At 30 hrs.—Pressure, 105 cm. water; W.B.C., 10,200; P.M.N., 86%.

Waves bigger. Appendix more blanched than earlier.

No necrosis evident.

At 42 hrs.—Pressure, 108 cm. water. Almost no waves now.

W.B.C., 8,300. There was a pressure peak lasting ten minutes after taking blood for W.B.C.

At 44 hrs.—Pressure, 96 cm. water; temperature, 100.8° F.

At 47 hrs.—Pressure, 100 cm. water; temperature, 101.2° F. Still vague abdominal aches.

At 49 hrs.—Pressure, 105 cm. water; W.B.C., 13,000; P.M.N., 94%.

At 49½ hrs.—Pressure released. No change in abdominal pain. Volume elasticity determination showed no demonstrable stretching of the lumen.

Still 0.17 cc. at 100 cm.

At 50¼ hrs.—Temperature, 98.6° F.

At 62 hrs.—Temperature, 100° F.; W.B.C., 7,200; P.M.N., 92%.

*Ultimate Outcome.*—Colostomy was performed for obstruction due to spread of cancer of cervix uteri.

**Case 5, Table I.**—C. P., age 56. Obstruction and exteriorization of appendix followed by incannulation for recording pressure.

After 16 hrs.—The pressure had risen to 90 cm. water with waves up to 95 to 130 cm. coming every 10 to 15 minutes, the high points being climaxed by a spike. Careful questioning of the patient showed that he had sharp severe pains coming just as the pressure commenced to rise for each of these peaks, reaching its climax about two-thirds of the way up to the peak and ceasing just as the pressure commenced to drop. This was right lower quadrant pain. Just as it

ceased each time (after lasting 20 to 30 seconds) the patient had a pain in the left side in the region of the Mikulicz exteriorization of the carcinoma. Slightly more severe and evidently of the same nature (Fig. 6).

*Ultimate Outcome.*—Bloch Mikulicz resection of carcinoma of sigmoid. Recovery.

**Case 6, Table I.**—U. T., age 53. Obstruction and exteriorization of appendix followed by incannulation for recording pressure. The mesentery was too short to allow stretching the organ out straight and it was, therefore, kinked on itself in and just above the muscle layers of the abdominal wall.

At start—volume-elasticity determination D.4 cc. at 120 cm. water pressure.

After 16½ to 18½ hrs.—Pressure rose from 19 to 72 cm. water in a few small and one large jump suggesting that at this point fluid passed the kink.

At 19½ hrs.—Pressure, 73 cm. water; temperature, 100.2° F.

Pulse waves visible from this point onward.

At 20½ hrs.—Pressure, 74 cm. water; W.B.C., 13,000; P.M.N., 82%.

At 23½ hrs.—Pressure, 85 cm. water; temperature, 102° F. No pain at any time.

At 25½ hrs.—Pressure, 86 cm. water; temperature, 101.6° F.; W.B.C., 15,000. Pressure released; no change in sensations resulted.

Volume-elasticity determination at end of pressure recording—0.13 cc. at 120 cm. of water pressure.

At 29 hrs.—W.B.C., 11,000; P.M.N., 76%.

At 32 hrs.—Temperature, 101.6° F.

At 36 hrs.—Temperature, 100.8° F.

At 40 hrs.—Temperature, 100° F.

*Ultimate Outcome.*—Failed to return for posterior excision of rectum.

**Case 8, Table I.**—M. K., age 54. Obstruction and exteriorization of appendix followed by incannulation for recording pressure.

Barium in lumen from 24 hrs. before start—W.B.C., 10,000.

After 6½ hrs.—W.B.C., 13,200.

At 8¾ hrs.—Pressure, 51 cm. water.

At 24 hrs.—Pressure, 45 cm. water.

At 25 hrs.—W.B.C., 12,800.

At 26 hrs.—Waves begin to appear. Peaks come every 20 mins. and there are sharper waves between. The basal level rose gradually to 56 by 30 hrs.

At 30 hrs.—Sudden drop in pressure to 26 cm. with loss of waves suggesting rupture. Temperature, 101° F. No leak, however.

At 32½ hrs.—Pressure, about 20 cm.; W.B.C., 8,600. Pressure released. The temperature returned to normal in a few hours thereafter.

*Ultimate Outcome.*—Resection of carcinoma of sigmoid colon. Recovery.

#### *The Secretory Activity of the Obstructed Cecal Appendage in Animals.*

*Rabbit.*—Two years ago, it was reported<sup>10</sup> that rupture of the rabbit's cecal appendage attended luminal obstruction quite regularly. In about 75 per cent of instances perforation occurs within 10 hours after ligation of the base. The highest secretory pressure that has been observed to date (136 cm. of water) followed luminal obstruction of the cecal appendage in the rabbit. A large number of observations have been made upon rabbits, and failure to secrete has not yet attended obstruction.<sup>4</sup> The character of the secretions may be modified, however, by regulating the pressure at which secretion occurs.<sup>8</sup>

*Other Animals.*—The secretory behavior of the cecal appendage of a large number of other animals has been investigated, including most of the domestic animals as well as fowl, carnivorous mammals, rodents and monkeys. No

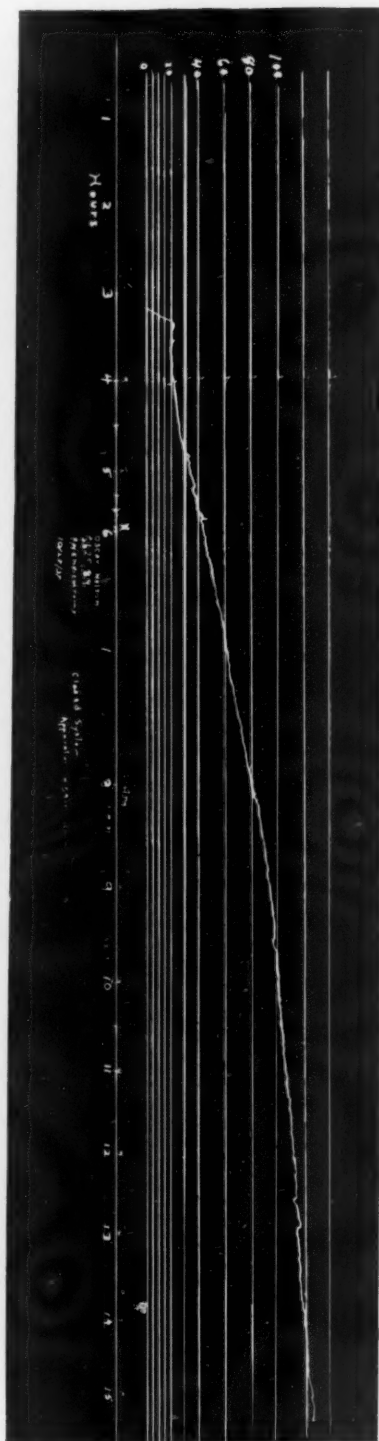


Fig. 5.—Pressure tracing of O.N., Case 2, Table I. A pressure of 125 cm. water was reached 14 hours and 15 minutes after obstruction.

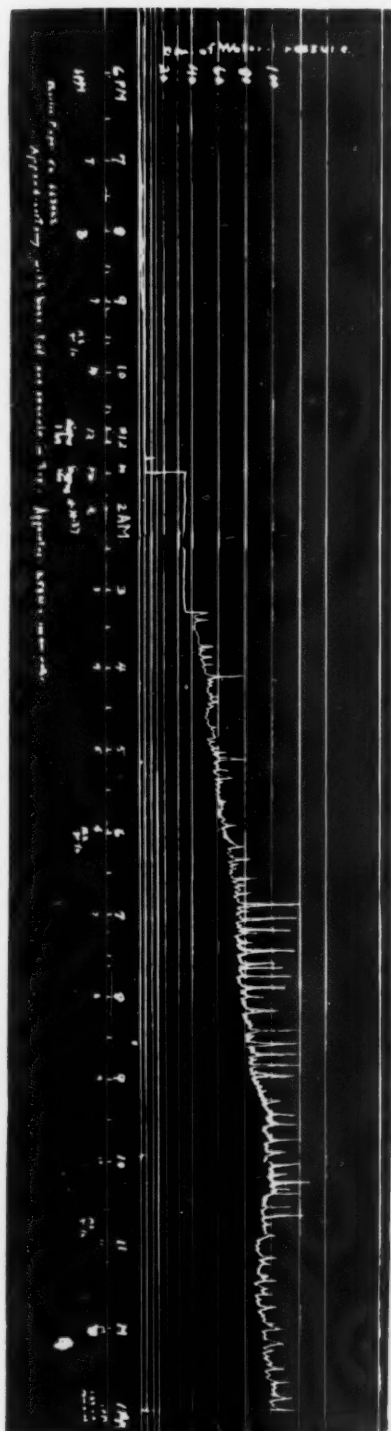


Fig. 6.—A. Pressure tracing of C. P., Case 5, Table I. A pressure of 90 cm. water was reached 16 hours and 30 minutes after obstruction.

evidence of secretory activity in the obstructed cecal appendage was noted in any of these.<sup>3</sup>

*Anthropoid Apes.*—The secretory activity of the vermiform appendix has been studied in two species of anthropoid apes, the gibbon and chimpanzee.<sup>11</sup> The highest secretory pressure observed in two gibbons was 19 cm. of water and in neither instance was this maximal pressure sustained for long.

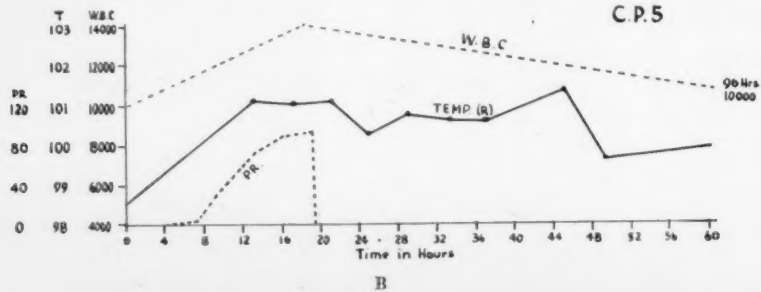


FIG. 6.—B. Chart indicating the leukocyte and temperature response incident to obstruction. (See details of case record No. 5.)

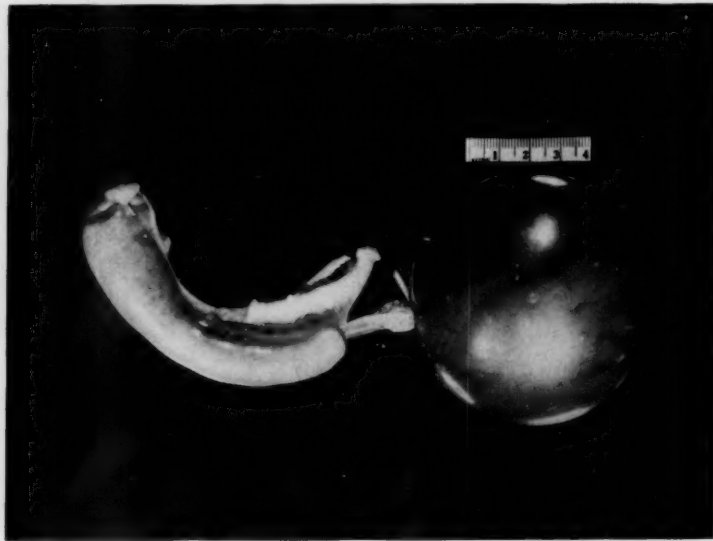


FIG. 7.—A. The obstructed cecal appendage of a rabbit from which fluid has been collected in a balloon. Two hundred cubic centimeters was collected in five days. The appendage is normal grossly and microscopically.

The vermiform appendix of the chimpanzee, on the contrary, exhibits a secretory pressure not unlike that of man and the rabbit. The highest pressure recorded in the obstructed appendixes of three chimpanzees was 106 cm. of water.

*The Nature of the Fluid Secreted by the Obstructed Appendix.*—Because of the small amount of fluid collectable from the obstructed vermiform

appendix of man, extensive observations on its nature have not been possible. The determinations made have been upon rather small quantities of fluid as is apparent from inspection of Table I. These would suggest that mineral salts such as calcium and phosphates may be present, as well as digestive enzymes. It is necessary, however, to rule out bacterial activity before concluding that digestive enzymes are present in the fluid.

Extensive observations have been made on the fluid secreted by the obstructed cecal appendage of the rabbit, however. About 20 cm. of fluid may be collected every six hours. Digestive enzymes are usually present in the fluid as it is collected in a small balloon within the rabbit's abdomen. After Berkefeld filtration to remove bacteria, however, no trace of proteolytic or other digestive enzymatic activity persists.<sup>8</sup>



B

FIG. 7.—B. Obstructed cecal appendage of a rabbit. Perforation occurred 5 hours and 18 minutes after recording was commenced, a pressure of 69 cm. water having been reached. Other areas of necrosis are apparent. This appendage showed evidence of diffuse cellular infiltration with areas of necrosis microscopically. (Reproduced from ANNALS OF SURGERY, 106, 927, 1937).

*Is the Fluid a True Secretion or a Filtrate?*—Whereas, no substance has been identified in the fluid which would stamp it definitely as a secretion of the mucosa of the appendix, there is every reason to believe that this fluid is secreted by the mucosa. First, fluid may be collected from the obstructed appendix at atmospheric pressure in both man and the rabbit (Fig. 7). Obstruction of the base of the cecal appendage in animals in which no secretory pressure develops is unattended by fluid secretion. Secondly, pressures attending obstruction of the appendix in man (126 cm. water or 92.6 Mm. mercury), chimpanzee (106 cm. water or 77.8 Mm. mercury) and the rabbit (136 cm. water or 100 Mm. mercury) have been observed to approach the systolic level of blood pressure. It has been remarked already that appendixes possessing an atrophic mucosa failed to exhibit evidence of fluid secretion (Table I). Observations made by Dr. C. J. Bellis,<sup>1</sup> in this clinic,



on the intraluminal pressures in spontaneously occurring appendicitis (obstructive) and the interstitial tissue pressures indicate that the intraluminal pressure distal to the obstruction, is higher in instances of acute appendicitis than is the interstitial pressure.

*Clinical Significance of the Secretory Capacity of the Appendix.*—The observations related above serve to emphasize the great importance of obstruction in the genesis of spontaneous appendicitis in man. The histologic picture of spontaneous diffuse appendicitis has been reproduced through the agency of obstruction alone. In the cecal appendage of the rabbit, all the varieties of appendicitis recognized by the pathologist from mere subserosal leukocytic invasion to gangrene or perforation may be produced by luminal obstruction.

That the rich lymphoid tissue of the vermiform appendix of man may play a rôle in initiating luminal obstruction in infections or other conditions which augment swelling in lymphoid tissue, is understandable. It would appear likely that this is the probable mechanism by which the lymphoid tissue of the appendix mediates its influence in causing appendicitis.

The usual causative agent in demonstrable obstruction of the appendiceal lumen is the fecalith.<sup>2</sup> How in turn it originates, still demands explanation.

It would appear necessary that the pathologist consider anew the obstructive concept of the origin of appendicitis. It is even more important that the clinician resurvey his concept of the early symptoms and findings of appendicitis. The dicta of Murphy; namely, pain, nausea and vomiting, abdominal tenderness, fever and leukocytosis, have been accepted almost universally as clinical desiderata of the disease. Appendicitis, however, is essentially a closed-loop obstruction in which the only early findings may be intermittent crampy pain and local tenderness. Elevation of temperature, quickening of the pulse and leukocytosis may not be in evidence until the anoxic effects of increased intraluminal pressure have set the infective characters of the disease in motion.<sup>9</sup> Finally, in order that the unwarranted mortality of the disease may be reduced more effectually, it would appear necessary to liberalize the indications for excision of the vermiform appendix. Appendicitis is probably still the most important of all surgical diseases. It ranks high as a cause of death and should be looked upon as a problem of the public health.<sup>9</sup>

#### CONCLUSIONS

The secretory activity of the vermiform appendix of man, possessing a normal mucosa, has been established. Such an appendix when obstructed and exteriorized may develop a secretory pressure approaching systolic blood pressure. The histologic picture of acute diffuse appendicitis has been produced in man by obstructing the exteriorized appendix. Appendixes having an atrophic mucosa fail to exhibit evidence of fluid secretion when obstructed. It appears likely that the chief inciting agency in bringing about appendicitis

in man is obstruction of an appendix in which the mucosa possesses the normal secretory capacity.

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## ILEOCOLOSTOMY WITH EXCLUSION\*

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Two of the most important developments in intestinal surgery during the last decade have been the increasing recognition of localized inflammatory disease of the terminal ileum and colon, and the trend in some surgical clinics toward stage procedures in the operative management of colonic neoplasms. As a result, ileocolostomy with exclusion is being more frequently performed either as a preliminary or definitive operation in inflammatory disease, and as a first-stage procedure in the resection of benign and malignant lesions of the right colon. The following communication is based upon the study of 32 cases of ileocolostomy with exclusion. This includes 16 cases of ileosigmoidostomy for regional ileitis and proximal regional hypertrophic colitis, three cases of ileotransverse colostomy for regional ileitis, and 13 cases of ileosigmoidostomy with ileocolic resection for malignancy of the right and transverse colon. Palliative anastomoses were not included as the period of survival was too short. These enterocolonic anastomoses were all routinely accompanied by transverse section of the ileum distal to the site of the anastomosis in order to completely exclude and short-circuit the intestinal flow from the diseased bowel. The technic followed has been to divide the terminal ileum between Payr clamps, carrying the incision well into the mesentery of the small bowel in order to secure the necessary independent mobility of the proximal and distal segments. Both ends were then closed by suture and continuity of the bowel was restored by a side-to-side enterocolostomy. No special attempt was made to perform an isoperistaltic anastomosis, the respective segments being placed along the axis in which they naturally lay. In lesions affecting the right and transverse colon, the ileum was divided about eight to ten inches from the ileocecal junction, great care being taken to preserve the integrity of the ileocolic vessels. In cases of nonspecific ileitis, the small intestine was divided through presumably healthy bowel at a point well proximal to the most oral segment presenting visible evidence of disease.

The operation as outlined above has always been preferred to ileocolostomy in continuity. The latter procedure is not infrequently complicated by trapping and stasis, factors which may produce marked distention and tension ulcerations of the loop of intestine between the enterocolic stoma and the area of diseased bowel. This complication, which may give rise to severe symptoms, has been emphasized by Estes and Holm,<sup>1</sup> and was observed twice in the course of secondary operations in which an ileocolostomy in continuity had been previously performed. Other disadvantages of this procedure are that secondary resections may be more difficult from a technical standpoint.

\* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

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Furthermore, in the presence of ileal or cecal fistulae intestinal leakage would still continue freely because the intestinal current had not been completely diverted.

The original gratifying results with ileocolostomy with exclusion were achieved in cases in which this operation had been primarily intended as a preliminary to later resection. The clinical improvement in many of these patients was so marked and the disappearance of intra-abdominal inflammatory masses and cutaneous fecal fistulae was at times so rapid, that we came to the conclusion that contemplated resection for inflammatory diseases should usually be performed in stages. The improvement following this relatively simple procedure has proven to be so great in numerous instances that resection in these patients has been indefinitely postponed.

Objections to ileocolostomy with exclusion have been raised on a number of grounds. The fear has been voiced that obstruction might produce sufficient back pressure to imperil the suture line of the distal excluded ileum. This complication has not been encountered in the present series. First, inflammatory disease rarely goes on to produce a complete obstruction. Second, the secretion of mucus and fluid requires only a very small channel to evacuate itself. In addition, malignant lesions of the right colon are rarely completely obstructive and in those cases in which acute obstruction has occurred, preliminary cecostomy has been performed. In cases of subacute obstruction in which there really is a doubt, the distal ileal loop may be brought out on the abdomen through a counter incision in a manner similar to the distal segment in the Lahey operation for carcinoma of the rectum.

Another danger which has been pointed out, is distention and possible perforation of the blind loop of ileum used in the side-to-side anastomosis. This danger is not peculiar to enterocolostomy with exclusion, but is equally present in cases in which intestinal resection has been performed. This possibility is a real one. It can be avoided by taking pains either to carry the line of anastomosis almost up to the blind end or by performing an end-to-side implantation of the ileum into the colon. In the present series, we have encountered what we take to be two instances with such dilated blind ends, which could be demonstrated clinically; in one case, by the palpation of a large sausage-shaped mass, and in the other, by roentgenographic evidence. In a third instance, the formation of tension ulcers in the blind loop produced symptoms of peritonitis which required surgical intervention. This patient had been operated upon about two years previously, at which time an ileosigmoidostomy with exclusion had been performed for a hypertrophic colitis involving the transverse colon. The patient improved markedly following the operation and had practically no gastro-intestinal complaints. Twenty-four hours before readmission, he complained of sudden, severe lower abdominal cramps, and vomited. Physical examination revealed temperature of 101° F., marked direct tenderness and rigidity in the right lower quadrant, and rebound tenderness throughout the lower abdomen. There was a moderate leukocytosis and the general picture was one of an acute appendicitis. Immediate exploration revealed the presence of a moderate quantity of seropurulent,

nonodorous fluid in the lower abdomen and pelvis. The appendix was normal. The cecum, ascending colon and terminal ileum were atrophic. Further exploration revealed that the blind loop of the ileum which had been used in the enterocolostomy was distended to about twice its normal size. The blind loop was about three inches in length and showed two areas about the size of a dime which were covered by exudate. Palpation revealed that these areas were markedly thinned. Resection of the blind loop was performed at a point about three-quarters of an inch distal to the stoma. The opening was then closed in layers. The pathologic report was "dilated ileum with two tension ulcers." The patient made an uneventful recovery and has remained well to date.

A third possible objection which has been voiced, especially in cases of ileosigmoidostomy, is that emptying of the fluid contents of the ileum into the sigmoid would result in diarrhea and might even prove irritative to the lower sigmoid and rectum. Such a diarrhea has not been observed in any case in which the sigmoid was found to be normal at the time of operation. As a matter of fact, in the right-sided colitis and ileitis the diarrhea which was previously present has disappeared. In a number of instances previously discharging perianal fistulae, instead of becoming aggravated, healed. There has been no impairment of control or development of any proctologic symptoms.

Fourth, the most frequent objection encountered has been that in the presence of such a long, blind, excluded loop of colon, stasis, retention, distention and ulceration might result in the segment of colon lying between the ileocecal region and the site of anastomosis. Here, again, clinical, radiologic and operative observations have brought no evidence which would tend to confirm such a belief.

The altered morphologic and physiologic conditions which resulted from ileocolostomy with exclusion have been carefully studied. The physiologic alterations were noted by careful, repeated inquiry into the nature of the patient's gastro-intestinal symptoms and activities. Thirty-two patients, 22 of whom have been followed for more than three years, were subjected to personal interviews and examinations. Results of this investigation may be summarized by saying that intestinal function following any of the above mentioned operations did not vary greatly from normal. The patients' appetites were good. Most of them had gained weight, some of them enormously so. With few exceptions they reported that after a few weeks they were having a maximum of three stools per day, and some were having only two movements, which were more or less normal in consistency, usually being described as "mushy" or "soft." They were neither diarrheal nor scybalous. Abdominal cramps were absent and defecation was as a rule unaccompanied by any dyschesia. Control was normal and when the desire to defecate overtook them at an inopportune time the desire passed away following inhibition. Most of these patients have only very rarely to resort to either cathartics or enemata. The only constant abnormal symptom complained of by these



patients, in approximately more than half the cases, was borborygmus and rumbling in the abdomen. This varied from a relatively minor symptom to a point where it became embarrassing in public. Another variation, which is perhaps worthy of note, was that dietary indiscretions were more apt to be followed by diarrhea. Incidentally, we may state that no attempt has been made to keep these patients on any specific diet. They have more or less eaten what they liked. In two instances symptoms were definitely traced to overeating of unusually large quantities of fruit or vegetables which produced frequent but not distressing bowel movements, in one case, and flatulence in another. It probably would be better policy to limit types of food tending to produce fermentation in the colon, and this, perhaps, might reduce the tendency toward excessive flatulence.

It is the authors' belief that a relatively small blind loop on the ileal side distal to the anastomosis is much more apt to show signs of dilatation and ulceration than is the unilateral excluded colon. This is probably due to the fact that retrograde peristalsis is present in the colon as a physiologic function, and that when an impulse is received distally, the colon can respond by emptying itself in the normal direction.

In order to visualize the mechanics of bowel function and to study morphologic changes which might be present, roentgenologic studies following a barium meal were made in 22 cases. By giving a barium meal it was possible to trace the course normally taken by the intestinal contents. These studies revealed that following ingestion of barium the medium commenced to reach the stoma within four to six hours. It was found that the ileal loop directly proximal to the anastomosis or immediately adjacent to it was dilated in almost one-third of the cases. Except in two cases, this dilatation was not accompanied by any tendency to stasis, and may be a manifestation of physiologic accommodation. In two instances, however, definite evidence of gas accumulation and retention of barium in the loop of ileum could be determined. In one of these cases, there had been an unusual dilatation of ileum noted from the onset of the patient's illness. This was a female, age 26, who was admitted to the hospital with acute, complete intestinal obstruction of about three days' duration. Study revealed that this was due to an obstructing lesion at the hepatic flexure for which a cecostomy was performed. At this time, enormous dilatation of the terminal ileum was noted. Three weeks later, an ileosigmoidostomy with exclusion was performed. In spite of the free drainage in the interim the marked distention of the ileum had not abated. At the final resection, a few weeks later, the continued dilatation of the ileum was again noted. In this instance, the distention of the ileum has apparently never returned to normal. The mechanism in the other case with this type of ileal stasis does not appear clear. All that can be said is that it was not giving rise to any clinical symptoms.

After passing the ileocolic stoma the barium stream was seen to pass both ways; part of it passed distally with normal peristalsis, and another portion, usually about equal in amount, was carried up the excluded proximal

colonic segment by retrograde peristalsis. The level to which retrogression occurred was determined by the site of the inflammatory lesion. In cases of inflammatory disease in the transverse colon, the barium was usually carried back to the region of the splenic flexure. In lesions in the right colon it passed, as a rule, to the level of the proximal transverse colon. In some cases of ileitis it was carried back as far as the cecum. The stream which passed distally was not expelled immediately. At the 12- and 24-hour observations it was found that most of the distal barium had been expelled. Some of the barium which had passed into the blind colonic loop by reverse peristalsis remained from 48 to 72 hours. Preliminary plates of the abdomen showed no marked gaseous distention in the excluded loop of colon. It is interesting to note that after the barium had passed into the colon there was never any demonstrable retrograde passage into the terminal ileum.

In a number of instances studies were made following a barium enema. Both the barium meals and barium enemata showed no abnormal dilatation or distention of the excluded colon, and haustrations and sacculations were normal, even after years of unilateral exclusion. When a barium enema is administered there is, as a rule, retrograde passage through the ileocolic stoma as well as into the excluded loop of bowel. Furthermore, the force of the barium enema is sufficient to carry the contrast medium to a point much farther proximal to the diseased segment than ordinary retrograde peristalsis. The only instance in which barium was trapped and became scybalous, was the result of such retrograde passage in the case of hypertrophic colitis.

Further opportunity of studying the physiology of the excluded colonic loop following ileocolostomy was afforded by two cases with fecal fistulae. In one of these, extensive obstructive resection had been performed for a carcinoma of the transverse colon in a very obese woman. An attempt to close the resultant artificial anus extraperitoneally was only partially successful, a small opening in the bowel remaining. An ileosigmoidostomy with exclusion was then performed to short-circuit the intestinal contents. This patient was examined on a number of occasions. It was found that the stool which could be observed in her transverse colon was solid. In another patient, an ileotransverse colostomy was performed for a large, prolapsing cecal fistula. Although there was considerable diminution of fecal drainage, a certain quantity of semisolid stool would appear at the cecal opening. Both these cases demonstrate that retrograde peristalsis with the functioning of the absorptive power of the colon takes place.

From a comparison of the bowel function following ileotransverse colostomy and ileosigmoidostomy with exclusion, no definite differences could be elicited. In summary, therefore, it would appear that the contents of the small intestine upon entering the colon at once pass in a retrograde direction to a certain extent. Whether there is any further retrograde extension of the material which originally passes into the distal loop cannot be stated. In any event, there is sufficient retrograde extension to permit of the normal absorptive functions of the colon to occur, and to render the stool solid or

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semisolid. The occurrence and extent of this retrograde peristalsis is important to bear in mind if a short-circuiting procedure is performed for a type of regional colitis affecting the splenic flexure and descending colon. In such instances, ileosigmoidostomy alone is probably insufficient to protect the diseased bowel from the intestinal contents. In this type of case, division of the colon just proximal to the anastomosis must be performed as recommended by Berg<sup>3</sup> and von Beck.<sup>4</sup> Further evidence that there is no unusual dilatation or stasis in the excluded loop of colon was obtained in five instances by secondary operation, all following a period of at least a year, and, in two cases, for periods of more than five years. No abnormal dilatation, distention, thickening, or atrophy of the excluded loop could be appreciated.

The question may arise as to why ileosigmoidostomy rather than ileotransverse colostomy was performed in such a large percentage of cases. In the first place, it seemed logical to assume that because of the tendency to retrograde peristalsis, much better exclusion of the diseased segment of bowel could be obtained. Second, in carcinomata, especially near the hepatic flexure, it was felt that if necessary, more radical resection because of lymphatic node involvement could be carried out, and if necessary the main branch of the middle colic artery could be divided. Third, experience has shown that in cases of right-sided hypertrophic colitis it might not be possible to absolutely ascertain that the anastomosis was being performed in a healthy segment of transverse colon. Fourth, in cases in which fistulae were present it seemed obvious that less opportunity for leakage of intestinal contents would occur, the more distally the ileocolic anastomosis was placed. Fifth, the lateral anastomosis appeared to be technically safer and simpler to perform in the more muscular sigmoid than it was in the transverse colon with its sacculations and haustrations.

In regional ileitis, however, experience with recurrences proximal to the line of anastomosis has led us into more frequently performing ileotransverse colostomy. In such cases a secondary exclusion operation can be performed by dividing the ileum proximal to the diseased area and then anastomosing the bowel with the sigmoid.

It is our opinion that the physiologic alterations produced by ileocolostomy with exclusion are not sufficient to give rise to any pathologic symptoms, with the exception of possible distention and ulceration caused by leaving too long a segment of small intestine beyond the area of anastomosis. Occurrence of intestinal symptoms, such as abdominal cramps and persistent diarrhea, has, in our experience, been due to a recurrence or extension of disease in the bowel. In instances in which the primary operation has been undertaken for lesions in the ileum, the symptoms have been found to be due to recurrence of the disease in the ileum proximal to the site of anastomosis. In cases of primary colonic disease, recurrence of symptoms has usually been due to persistence of the disease or extension to a more distal segment of colon. This possibility has been avoided by limiting this type of operation to the definitely localized granulomatous, hypertrophic types of colitis.

In this regard, it is of interest to cite a case operated upon on the service of Dr. Richard Lewisohn and previously reported by him.<sup>2</sup> In this patient, ileotransverse colostomy with exclusion was performed for an extensive terminal ileitis. For a few months the patient was considerably relieved but recurrence of diarrhea forced her readmission. At this time, the previously excluded loop of ileum as well as cecum were resected. They showed marked regression in the pathologic findings. For a while the patient's symptoms again subsided but episodes of abdominal pain and diarrhea again recurred. Roentgenologic examination at this time revealed a lesion in the small bowel just proximal to the stoma, which was again resected and an ileosigmoidostomy was performed. Since that time, this patient has again had recurrence of symptoms and again a lesion proximal to the anastomosis has been discovered roentgenologically. It is interesting to note that at the time of the resections, in neither instance did the excluded loop of bowel show any marked changes.

One drawback to ileosigmoidostomy and subsequent resection, as above described, occurs in cases of malignant disease, because either a recurrence or development of a new tumor in the blind loop of bowel will, at first, be practically symptomless. In one such instance, the only symptom of a neoplasm, that occurred in the blind loop, was a rapidly developing anemia. In this patient, an ileosigmoidostomy had been followed by a wide resection of bowel, carried from the terminal ileum to the transverse colon for a double carcinoma of cecum and hepatic flexure. The patient was seen about one year later with a history of weakness and anemia. The stool was strongly positive for blood. Barium enema showed a filling defect in the transverse colon where a new tumor had apparently developed. However, if careful track is kept of the patients with malignant disease and an early diagnosis is made, further resection in these cases of multiple carcinomata is simpler than if an ileotransverse colostomy is present.

There are certain technical features which may perhaps be emphasized: In the first place, it has become our custom to perform the ileocolostomy through a left-sided incision. We found that this permits an adequate exploration and exposure of the ileocecal junction. The advantage of the left-sided incision is that secondary procedures on the right colon are rendered much more simple, technically, as massive adhesions sometimes develop in the operative field. Furthermore, there is a certain sense of security, and undoubtedly more healing power, resulting from a fresh wound than that following the reopening of an old one. Also, if infection of the wound should occur when the left rectus incision is used, the second stage will not be held up too long. Infection of a right-sided wound might delay such a secondary resection for a considerable length of time.

We cannot emphasize too strongly the necessity of visualizing the ileocecal junction and being positive that it is the proximal portion of the divided bowel which is being anastomosed. We know of instances in which the distal loop has inadvertently been the seat of the anastomosis. Another difficulty which deserves mention and which can be circumvented by proper technic, is

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the occurrence of adhesions of the blind loops to each other or to the stoma. To avoid this, we have at times excised a small segment of ileum and inverted the distal closed end into the distal ileum to a greater extent than usual. However, we have found that if division of the mesentery is carried far enough down, the necessary independent mobility will usually be achieved. Incidentally, it is our belief that too long a blind loop is much more apt to be left behind, distal to the ileocolic anastomosis, if division is practiced at the second stage rather than the first. In such cases one hesitates to approach too closely to the relatively fresh stoma; and the frequent presence of inflammatory induration in the immediate vicinity of the anastomosis also tends to lead the operator to divide the ileum more distally.

### SUMMARY AND CONCLUSIONS

A group of 32 cases of ileocolostomy with exclusion are reported. Clinical, roentgenologic, and operative studies in this series revealed:

(1) That obstruction and dilatation of the distal excluded ileum did not occur.

(2) That in the case of ileosigmoidostomy there was no irritative effect on the lower bowel.

(3) That, although there was retrograde passage of ileal contents into the excluded segment of colon, there was no abnormal distention, dilatation or ulceration of this loop.

(4) The only site at which definite pathologic alterations occurred as a result of the operative procedure, was in the blind end of terminal ileum used in a side-to-side anastomosis. In two cases, there was marked distention of this blind end and in one case tension ulcers produced peritonitic signs necessitating resection of the blind loop.

(5) The operation of ileotransverse colostomy or ileosigmoidostomy with exclusion does not in itself produce symptoms. Recurrence of symptoms has been found due to recurrence of the disease proximal to the anastomosis when the original operation was undertaken for disease of the small intestine. In cases in which the operation was performed for the localized type of colitis, symptoms have been found to be due to either persistence of the disease in the excluded loop of colon or its extension distally.

(6) In view of the fact that ileocolostomy with exclusion does not produce any untoward gastro-intestinal symptoms, it might be advisable to use this procedure as a first-stage operation for inflammatory diseases of the right colon and terminal ileum. The necessity for further intervention could then be judged by the future course of the disease.

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DISCUSSION.—DR. JOHN DEJ. PEMBERTON (Rochester, Minn.): I would like to discuss very briefly one or two points regarding ileitis: In December, 1936, I reported all the cases of regional enteritis seen at the Mayo Clinic in the 15-year period 1922 to 1936, inclusive. There were 39 cases, and at that time I attributed the increased incidence in recent years to an increased alertness on the part of the clinician and the roentgenologist in recognizing the disease. However, in the past 30 months we have seen 68 cases, that is, there have been almost twice as many cases in the last three years as in the prior 15 years. I now feel, very definitely, that the disease is on the increase.

Because of this fact and because we know very little, or nothing, regarding the cause, I think it is exceedingly important that this subject be repeatedly brought to the attention of the profession.

Our experience has led us to believe that the best treatment for regional ileitis is the resection of the affected segment or segments involved, either in a one-stage or two-stage procedure, depending upon the conditions found in the individual case. When a two-stage procedure is employed because of the presence of a fistula or of the poor general condition of the patient, I believe that a period of two to six months should elapse between the stages. This allows, of course, for the rehabilitation of the patient as well as for a partial resolution of the inflammatory process. I do not believe that the period should be longer than six months, because of the risk of extension of the inflammatory process.

In many of our cases, because of marked improvement obtained following ileocolostomy or a short-circuiting procedure, we have delayed the second operation for several years; in some this has been delayed as long as five years. In none of these cases have we seen complete resolution, but on the contrary, in several of the cases we have seen definite extension of the process to involve the ileum at the site of anastomosis or proximal to the site of the anastomosis.

There is another reason why I think it is important to resect the infected part of the ileum; this is because the process sometimes is tuberculous, and yet it is indistinguishable grossly from the nontuberculous type of ileitis. I recently operated upon a patient, upon whom I had performed an ileocolostomy six months before, for what was thought to be nontuberculous enteritis, but the pathologist found that the lesion was tuberculous.

TABLE I

CASES OF REGIONAL ENTERITIS IN WHICH OPERATION WAS PERFORMED FROM  
JANUARY 1, 1922, TO APRIL 30, 1939, INCLUSIVE

No. of Cases	Surgical Procedure	Hospital Deaths	Mortality, Per Cent
6	Abdominal exploration* . . . . .	1	16.7
30	Exclusion or short-circuiting operation . . . . .	6	20.0
32	One-stage resection and anastomosis . . . . .	2	6.3
39	Two-stage anastomosis and resection . . . . .	1	2.6
Total 107		10	9.3

\* One case, enterostomy; one case, drained and closed fistula.

Table I shows the cases of regional enteritis seen in the clinic from January 1, 1922, to April 30, 1939, inclusive, of which we have definite record. Parenthetically, cases of lesions of the small bowel seen prior to 1922 have not been reviewed. The cases listed under abdominal exploration were, for

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the most part, cases in which the lesion was very extensive and in which no major surgical procedure was performed. The mortality rate in the exclusion operation was high, not because the operation in itself was more hazardous than the operation of resection but because of the very poor condition of the patients. There were two deaths in the group of 32 cases in which resection was carried out in one stage. The group was comprised, of course, of selected cases. I think it is particularly interesting that of the 39 cases in which resection was carried out in two stages there was only one death. It seems to me, therefore, that, if the patient can endure a preliminary ileocolostomy, resection of the affected segment of bowel should be performed later, since resection can be accomplished at small risk.

DR. VERNON C. DAVID (Chicago, Ill.): The essayists have discussed the subject of ileocolostomy with thoroughness, and have raised a number of interesting technical and physiologic problems for discussion.

As to the indications for ileotransverse colon colostomy, I would hazard the opinion that they are much the same in all clinics. During the last three years at the Presbyterian Hospital, Chicago, the operation was carried out 27 times (Table I).

TABLE I

Carcinoma of the cecum and ascending colon....	10
Carcinoma of the hepatic flexure.....	2
Carcinoma of the ileocecal valve.....	1
Lymphosarcoma of the cecum.....	3
Postoperative obstruction after appendicitis....	2
Granuloma of the cecum.....	1
Intractable fistula of the cecum.....	1
Terminal ileitis.....	7

Total 27

There were five deaths in this group, all of whom had a tumor, one from embolism and four from peritonitis; three of these deaths occurred in inoperable cases where the operation was performed to relieve obstruction.

The title "Ileocolostomy with Exclusion" raises the question as to whether an ileocolostomy should always be performed after division of the ileum as the authors indicate. We practically always perform the operation without division of the ileum when the operation is undertaken to relieve obstruction or purely as a side-tracking procedure, and have had reason to believe that the new and wide lateral anastomosis between the ileum and transverse colon actually did side-track the fecal stream. I would like to cite one informative case:

A large cecal fistula, following accidental injury during a nephrectomy, persisted in spite of repeated efforts at closure. An ileocolostomy in continuity produced a dry and practically feces-free field which allowed prompt healing of the fistula after operation. The efficacy of the operation in terminal ileitis is more difficult to estimate due to the tendency for the disease to have multiple and often recurrent lesions, developing months or years apart. We believe with the essayists that a side-tracking operation as the first-step procedure in terminal ileitis, especially if a fistula is present, is a sound procedure.

The question of a one- or two-stage operation in carcinoma of the cecum, ascending colon, or hepatic flexure, must be left to the individual operator's judgment, all agreeing that obstruction, adiposity, poor cardiovascular quotient, or marked local inflammatory reaction about the tumor should call for

a preliminary ileocolostomy. Wherever possible, however, we believe in the one-stage operation with a wide lateral anastomosis between the ileum and transverse colon in preference to the end-to-side aseptic method.

I should like to call attention to the possibility of a carcinomatous implant at the site of the anastomosis in a two-stage operation. That implants take place, is rather dramatically evidenced in a patient who had had an extensive horseshoe rectal fistula for five years, upon whom several operations had been performed and several biopsies made, all showing chronic inflammatory tissue. At the last operation, the lining of the fistulous tract was friable and a biopsy showed it to be a papillary adenocarcinoma. On questioning the patient, he admitted having had rectal bleeding for three months. Proctoscopic examination showed a small papillary carcinoma 15 cm. above the anus. We have had another patient who developed a small carcinoma at the junction of the skin and the mucosa of a colostomy performed as a preliminary first-stage operation for carcinoma of the rectum. While implantation of carcinoma at the site of an ileocolostomy is undoubtedly rare in the two-stage operation, it must be considered as a relative indication for the one-stage procedure.

The essayists' remarks on ileosigmoidostomy were very interesting to me, in that they have observed no tendency for the patient to have liquid stools resulting from retrograde passage of the fluid contents of the ileum into the ascending and transverse colon. I have avoided the operation wherever possible because of the supposed tendency to diarrhea, and would still be inclined to employ an ileotransverse colon anastomosis wherever possible, as it physiologically places the liquid contents of the small loop as far to the right in the colon as possible and excludes the dangers of a large blind loop.

DR. RALPH COLP (closing): There is very little that I can add except to reiterate that the cases in which an ileosigmoidostomy with exclusion has been performed have not complained of diarrhea after the first few weeks, and if they did complain of diarrhea at a subsequent period, it could be taken for granted that there was some extension of the disease.

## THE VALUE OF PRELIMINARY COLOSTOMY IN THE CORRECTION OF GASTROJEJUNOCOLIC FISTULA\*

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OVER THE YEARS there have appeared in the literature instances of spontaneous fistulous communications between stomach, duodenum, jejunum and colon in varying combinations, produced by a variety of lesions such as gastric or colonic carcinoma, abdominal tuberculosis or pyogenic abscess, ulcerative colitis, trauma and unoperated ulcer of the stomach or duodenum, the last such case being reported by Wilkie.<sup>1</sup> However, following the employment of gastro-enterostomy for ulcer in cases which we now know were unsuitable, the formation of a gastrojejunal or jejunal ulcer was not infrequent, and in a number of cases, by adhesion and continued erosive action, a communication was made between the stomach, jejunum and colon—the gastrojejuno-colic fistula.

Just as the etiology of peptic ulcer is not definitely known, so the cause of these new ulcers at or just beyond the stoma is not understood or controllable. The first such ulcer was reported by Braun,<sup>2</sup> in 1899. The frequency of occurrence varies widely in different statistics. Lahey<sup>3</sup> found the discrepancy to range from 1.7 to 24 per cent after gastro-enterostomy, and from 0.4 to 10 per cent after gastric resection. Lahey and Swinton<sup>5</sup> recommend two technical points which are probably of value in prevention; namely, the avoidance of entero-enterostomy and of occlusion of the pylorus. But it is evident that the problem is not one of technic alone. It is agreed that gastro-enterostomy in the young, sthenic, hyperkinetic, hyperacid type of individual is unwise because of the danger of subsequent ulcer occurring at the stoma.

In order to prevent the still more serious state which ensues when the ulcer perforates into the colon, it is recommended by some to make an anterior gastro-enterostomy; or if a posterior gastro-enterostomy is made, to place the opening in the transverse mesocolon near the base rather than near the colon.

Czerny, in 1903, reported the first case of gastrojejuno-colic fistula following gastro-enterostomy. Since then, a considerable number of cases have been reported in the literature, either as isolated case reports or in small series. They may occur within the first year after gastro-enterostomy or only after many years have elapsed. They may be small or large and may be direct or through the medium of a fistulous tract, usually short. The symptomatology and diagnostic signs have been constructed. These consist of: (1)

\*Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

Pain, not necessarily of ulcer character, and as in primary ulcer, inconstant and sometimes inconspicuous or absent; (2) diarrhea, with symptoms simulating colitis resistant to medication and diet, and the passage of undigested food recently taken by mouth. This has been thought to be due to direct passage of food from stomach or jejunum into the colon but we believe, on the basis of fluoroscopic findings, that it results from the exceedingly rapid transport of food through the stomach and intestines and is probably due to the irritation of the tract from the presence of colonic contents in the stomach and bowel (ref. roentgenologic examination of Case 2); (3) eructation of foul gases and vomiting of material obviously resembling colonic contents often occur; (4) general responses are loss of weight and strength, frequently extreme, with anemia and blood protein disturbances.

Such symptoms, when seen in characteristic form, make the diagnosis extremely probable. Roentgenologic examination is always advisable in doubtful cases and for verification in all cases. Deformities, extreme hyperperistalsis extending throughout the small intestine, the visualization of the fistulous tract or the actual passage of opaque mixture from colon to stomach or vice versa, are the suggestive or positive signs.

The treatment of anastomotic ulcer by medical management is not so successful as is that of primary gastric or duodenal ulcer, and the results are more difficult to check. Unless a satisfactory measure of success is obviously forthcoming, it would seem wiser to reoperate upon these cases and carry out an extensive gastric resection. When fistula has once formed, it might almost be said that there is no medical treatment. It has been the general experience that diet, alkalies and other adjuncts have little or no favorable influence upon a fistula once established. Delay results only in further deterioration of the patient as a surgical risk confronting an operation which is necessarily formidable.

The prognosis without operation is exceedingly grave. In most cases there is progressive inanition and early death from perforation, hemorrhage or intercurrent disease. On the other hand, operation has, hitherto, proved to involve great hazard. Loewy<sup>13</sup> discusses a collected group of 63 cases which were corrected surgically with a mortality of 27 per cent. Verbrugge<sup>6</sup> describes a group of 20 cases with operative mortality of 25 per cent. Allen<sup>14</sup> reports two deaths in eight cases (25 per cent). Lahey lost five out of eight patients, mortality 63 per cent, albeit but one died of peritonitis. On his recent visit to this country, Finsterer recounted his personal operative experience with one-stage gastroduodenal resection, which yielded five deaths in 13 cases (38.4 per cent). He quoted Gosset as having collected 28 cases with 12 deaths (42.8 per cent). From my personal knowledge of such cases operated upon and never reported, it seems probable that the total mortality is much higher than these figures. Personally, prior to adoption of the procedure herein advocated, my own experience, fortunately, comprised only two cases. Both died following one-stage operations, though the technical procedures were satisfactory and not attended by shock, hemorrhage or gross contamination. One died of peritonitis, the other of bronchopneumonia which he was unable



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to combat, though he lived four weeks after operation. Both were in bad general condition, having grown progressively worse over a long period of attempts at improvement under medical management. It seemed to me then, and it seems to me now, that any operation of magnitude performed upon subjects in such a low state of nutrition and resistance will inevitably be attended by a high percentage of complications and mortality.

It was with such a background that I encountered the following case in the Abington Memorial Hospital:

**Case 1.**—K. E., white, male, age 34, was seen first, September 14, 1936, complaining of severe diarrhea, voracious appetite, marked weakness and fatigue, and loss of 30 pounds. A gastro-enterostomy had been performed elsewhere four years previously, following which, he had been improved until the onset of his present symptoms, five months before.

*Physical Examination* revealed a pallid, emaciated man, with boggy, slightly distended abdomen and moderate tenderness in the epigastrium. On auscultation peristalsis was in a continual state of unrest. Slight pitting edema of the ankles was observed. There was a moderate hypochromic anemia. The urine was normal. Fractional gastric examination revealed a Grade 4 hyperacidity. Sigmoidoscopic examination was unsatisfactory due to a constant trickle of liquid, frothy feces containing mucus and particles of partially digested food. The mucosa was intensely congested but not ulcerated.

*Roentgenologic Examination.*—The barium passed out of the stomach too rapidly to permit of adequate study. Some went through the pylorus but the bulk left by way of the stoma. The stomach was completely empty in 15 minutes. All was passed along through the small intestine with great rapidity. No barium could be seen passing directly into the colon from the stomach. By barium enema this mixture was seen fluoroscopically to freely enter the proximal third of the stomach, directly from the distal part of the transverse colon, giving definite evidence of gastrojejunal fistula.

He was placed on ulcer regimen and sent home, but returned in two weeks with symptoms uninfluenced, and was given two transfusions in preparation for operation.

*First Operation.*—October 2, 1936: Considerable excess of clear peritoneal fluid was present. The scar of a healed anterior duodenal ulcer was noted. At the site of the gastro-enterostomy, the stomach, colon and jejunum were matted together and surrounded by adherent mesenteric structures and omentum, the whole forming a mass almost as large as a fist. Still more striking was the highly inflammatory state of the tissues. The adjacent gastric wall was edematous. The proximal and distal loops of the jejunum were greatly thickened and congested and showed shaggy exudate from the serous surface and actual small plaques of new fibrin. In addition to the fistula, there were two jejunal ulcers, one 2 cm., the other 8 cm., below the anastomosis. It was obvious that radical surgery could not be safely performed upon such tissues. Recalling that this fistula apparently worked in only one direction, that is, from colon to stomach, it occurred to me that preliminary colostomy might favorably influence the conditions present. Accordingly, a loop of ascending colon was brought out through a muscle splitting incision external to the semilunar line. The loop was opened on the third day and function promptly established. Recovery was uneventful. All symptoms disappeared. Nineteen days after operation, he was discharged with no digestive trouble, excellent appetite and gain in weight. He was having no movement by normal channels.

Three months later, January 25, 1937, he was readmitted for operation, having gained almost 50 pounds, feeling and looking well. He had had no evacuations by rectum. Roentgenologic reexamination showed barium leaving by way of the gastro-enterostomy into the jejunum but none into the colon. On barium enema, however, barium could be seen entering the stomach directly at the old site.

*Second Operation.*—February 1, 1937: The abdomen was reopened through the for-

mer left paramedian incision. The change in condition was truly unexpected and astounding. There was no excess peritoneal fluid. The inflammatory mass was smaller, the walls of both stomach and jejunum, in relation to the anastomosis, were normal in thickness and consistency and were uninflamed. Since the old duodenal ulcer was apparently healed and the pylorus patulous, it was decided to take down the anastomosis and make the necessary repairs to restore the normal anatomy. The stomach was disconnected and closed. The jejunum and colon were detached and repaired. Curiously enough, at this time there was no more ulceration at the site of the fistulous communication. The jejunal ulcers also had disappeared. The operation was somewhat extensive and time-consuming but was carried out upon good tissues and without danger of contamination from the colon.

Recovery was without incident except for extensive distention on the third day, for which a simple purse-string jejunostomy was performed under local anesthesia. On the tenth day, crushing of the spur of the colostomy was begun and completed six days later. The colostomy was closed (third-stage Mikulicz), March 9, 1937. Healing was prompt and no digestive symptoms remained.

Roentgenologic examination, March 22, 1937, showed irregularity of mucosal pattern of stomach, nonfilling duodenal cap, empty at three hours. Barium enema showed a normal somewhat hypotonic colon. Gastric analysis still showed hyperacidity, maximal in one hour, total 95, free acid 75. He was placed on ulcer regimen, returned home, and has remained well, pursuing his usual occupation as shoemaker.

Struck by these findings and the alteration in conceptions of the pathologic physiology thus suggested, and the possibility of lowering the high mortality of surgical treatment which seemed to be presented, another case was anxiously awaited.

**Case 2.**—R. B., white, male, age 29, was admitted to the Abington Memorial Hospital, June 3, 1938, complaining of diarrhea, fecal vomiting and belching of gas with fecal odor, diffuse abdominal pain and loss of more than ten pounds, all occurring within the preceding five weeks. He had had an appendectomy in May 1927. In August, 1929, a perforated duodenal ulcer was closed by simple suture. In February, 1937, a recurrence of duodenal perforation occurred and this time, in addition to closure of the perforation, a posterior gastro-enterostomy was performed. All these operations were performed by other surgeons. About five weeks following the closure of perforation and performance of a gastro-enterostomy, the patient began to complain of pain in the left lumbar region which persisted for six months and then subsided for eight months. About two months before present admission, the pain recurred in the left lumbar region but was most severe somewhat higher than previously. This pain was relieved temporarily by alkalies and food, and persisted for about one month, to culminate in the symptoms presented when seen in June, 1938.

*Physical Examination* revealed a pallid, undernourished male adult. Peristalsis was alternately ferocious and inaudible; abdominal tenderness was rather general in the upper quadrants but was most marked over a small area just below and immediately to the right of the umbilicus. Urinalysis, complete blood chemistry, blood Wassermann and Kahn were all negative. Blood counts revealed moderate secondary anemia. Barium administered orally was seen to leave the stomach through both pylorus and gastro-enterostomy, but easy flow of radiopaque medium was seen by way of a fistulous communication of the jejunum with the colon. Barium enema even more clearly revealed this communication through which radiopaque material passed easily from a point just proximal to the splenic flexure of the colon directly into the stomach and jejunum. Two preoperative blood transfusions were administered.

*First Operation.*—June 8, 1938: Under spinal anesthesia, celiotomy disclosed numerous adhesions of the omentum both to viscera and parietes. The posterior gastro-enteros-

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tomy could be visualized and the ascending arm of the transverse colon was found firmly attached to the anastomosis. The jejunum, both above and below the anastomosis, was seen to be dilated, thickened, reddened and edematous. This inflammatory process extended in some measure to the mesentery and to the attached colon. The ascending colon was mobilized and a loop colostomy was made through a stab wound in the flank. This loop of bowel was opened with the cautery five days later, and postoperative convalescence was uneventful. Three weeks postoperative, he was discharged to the care of the Gastro-Enterologic Clinic of the hospital. However, two days before discharge, the continued existence of the fistula was verified roentgenologically.

Four months after colostomy had been performed, the patient was readmitted. He had had no digestive disturbances and had gained greatly in weight. In the interval, there had been absolutely no diarrhea but there had been normal stools from the colostomy and some by rectum. The continued presence of the fistula was again verified roentgenologically. All evidence of secondary anemia had disappeared.

*Second Operation.*—Under spinal anesthesia, the site of the old gastro-enterostomy was exposed. The pylorus was patulous and the duodenal ulceration had apparently healed. The inflammatory changes in the jejunum and surrounding viscera noted at the previous operation were entirely absent. A jejunocolic fistula, measuring 3x1 cm., was found. The jejunum was dissected free and the opening in its wall closed. The defects in the colon and stomach were similarly closed, thus reestablishing normal continuity. A Stamm jejunostomy was performed just distal to the repaired area. The postoperative course was uneventful. The spur was destroyed and the colostomy opening repaired three and one-half weeks later, and the patient was discharged, five weeks after correction of the fistula.

He is continuing his ulcer prophylaxis regimen. Unfortunately his duodenal ulceration has become reactivated, and he has been urged to have a gastric resection performed, since he seems to fall into the group in which no operation short of this will prevent recurring peptic ulcer. Perhaps it would have been better judgment in view of this patient's history, to have done this instead of restoring normal continuity. In our opinion, it would have been feasible under the conditions present after preliminary colostomy but not before.

In February, 1938, I briefly reported the first case before the Joint Meeting of the New York Surgical Society and the Philadelphia Academy of Surgery. Shortly after this, Dr. Ralph Colp, of New York, adopted the suggestion and met with an even more striking evidence of the favorable influence of preliminary colostomy. He has been kind enough to furnish me with his notes on this case and to authorize me to use them here, for which I make grateful acknowledgment.

**Case Report.**—Dr. Ralph Colp: A male, age 49, was admitted to Doctor Colp's service January 7, 1935, and discharged January 24, 1935. He gave a nine-year history of ulcer type. Roentgenologic examination verified the presence of a penetrating duodenal ulcer with a large residue remaining after five hours. A retrocolic, posterior no-loop gastro-enterostomy was performed, followed by uneventful recovery and cessation of symptoms for three years. Three months before his second admission, April 13, 1938, he began to have frequent bowel movements accompanied by the belching of fecal-smelling gas. He had lost ten pounds. Barium enema revealed the presence of a gastro-jejunocolic fistula. A colostomy of the Mikulicz type was made with the ascending colon through a muscle splitting, right rectus incision. When the colostomy was established on the sixth day, almost immediately the patient observed that his breath was no longer foul. He was discharged symptom-free. After three months and a gain of 18 pounds, he was readmitted, July 8, 1938. The former fistula could no longer be demon-

strated roentgenologically. Barium in the stomach passed through the stoma into the jejunum but not into the colon. Barium enema injected through the colostomy showed irregularity of the midportion of the transverse colon but did not pass into the stomach.

*Operation.*—July 16, 1938: A hard inflammatory mass, the size of a lemon, which included the stomach, colon and jejunum, was revealed. About 12 inches from the duodenojejunal angle, the efferent jejunum seemed to be the seat of an ulceration. The fistula in the colon had evidently healed. The stomach was still much dilated. A partial jejunectomy with end-to-end jejunojejunostomy and a subtotal gastrectomy with a Hofmeister antecolic gastro-enterostomy was performed. The pathologic examination showed that the ulcer of the jejunum above noted had healed. After moderate reaction, the patient did well. Beginning two weeks later, the colostomy was repaired in the Mikulicz fashion. In March, 1939, the patient was seen and found well. He had gained 25 pounds.

In commenting on these cases, it is important to note that it is generally believed that in most cases of gastrojejuno-colic fistula there is a large loss of gastric contents into the colon, whereas actually in the first case there was no passage from stomach or jejunum into the colon but only in the reverse direction. The second case, however, was demonstrated roentgenologically to possess free flow in both directions by way of the fistulous communication. This was verified clinically, for colostomy resulted in no stool by rectum in the first patient, while in the second, stools were passed by rectum as well as through the artificial anus. This is important, for it lends forceful evidence to our belief that the devastating diarrhea seen in these patients is due to the presence of colonic contents within the upper intestinal tract, and that this can be controlled by diversion of the large bowel fecal current at a point above the fistula.

The choice of procedure is highly important in the surgical management of these patients. It has been pointed out that simple restoration of continuity has more adherents than the more radical corrective measures. We have no desire to enter into this question at this time, and we do not mean to imply that the use of restoration of continuity in these two instances indicates the nature of our preference in the matter. We do wish, however, to emphasize our belief that preliminary colostomy is compatible with any surgical plan in these cases and that it will undoubtedly prove of even greater value in those cases selected for the more radical procedures.

The effects produced by this procedure are apparently due to diversion of colonic contents from the stomach and small bowel. When the contents of the colon are being continuously regurgitated into the stomach and jejunum, the patient is continuously fed upon *feces*. It would seem that either by reinfection from the colon or by changes in gastric physiology, the anastomotic ulcer is continuously reactivated and that there is a definite tendency toward the formation of additional jejunal ulcers. It is worth noting that in Case 2, in which the fistula worked both ways, the discharge from the stomach into the distal colon after colostomy did not cause diarrhea or colitis, and did not interfere with nutrition. Small bowel movements occurred but in all essential respects the favorable effects of the preliminary colostomy were equal to those noted in Case 1, in which the fistula appeared to have a valve-like formation



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which allowed only the colon contents to enter the stomach and not vice versa. Clinically, the observations noted following this procedure were cessation of diarrhea with return of the patient to excellent physical state and hence reduction of the general risks of surgical intervention. Furthermore, the inflammatory reaction of adjacent tissues and the jejunal ulceration entirely subsided, thus reducing the risk of inflammatory complications in surgical correction of the fistula. A third effect of preliminary colostomy is freedom from contamination at operation and the later protection of suture lines in the repaired colon, abolishing the danger from leakage at this point.

It seems advisable to incorporate jejunostomy in the operation when the fistula is corrected, and this has been noted previously by Findley,<sup>15</sup> and Waters and Priestly.<sup>10</sup>

The use of cecostomy at the time of correction of the fistula has been reported by Bolton and Trotter,<sup>16</sup> Balfour,<sup>17</sup> and MacDonald,<sup>4</sup> and was recommended as a measure to protect the suture lines in the repaired colon, especially when such repair has been difficult. Exteriorization of the colon by some modification of the Mikulicz procedure has likewise been employed (Mason and Baker,<sup>18</sup> MacDonald,<sup>4</sup> Pauchet,<sup>19</sup> and Findley<sup>15</sup>). In their hands, the procedure was carried out at the time of the correction of the fistula and for the purpose of avoiding a suture repair of the colon with potential leakage and peritonitis. The single instance found in the literature in which either of the above procedures was employed as a preliminary measure to the correction of such a fistula was reported by Colucci,<sup>20</sup> and in this instance a cecostomy was performed upon a patient with symptoms suggesting intestinal obstruction. A gastrocolic fistula was later demonstrated and was apparently the result of spontaneous perforation of a gastric ulcer into the colon. No gastroenterostomy had been performed. Five months later, the fistula was corrected, and still later, the cecostomy closed. The same improvement in the patient's general condition and disappearance of clinical signs of intraperitoneal inflammatory reaction were noted by Colucci as were seen in the case we are reporting. This experience tends to strengthen the case for preliminary diversion of colonic contents from the upper gastro-intestinal tract. Who would doubt the superiority of loop colostomy over cecostomy in bringing this about? The question of the method to be employed in dealing with the ulcer problem presented at the second stage is beyond the scope of this paper. Recurrence of ulceration would seem to call for more radical procedures than simple repair and restoration of continuity. If so, preliminary colostomy offers a means of making the more complicated measures both simpler and safer.

### CONCLUSIONS

(1) Loop colostomy preliminary to correction of gastrojejunal colic fistula resulted in cessation of symptoms and return of the patients to their normal physical state, thus greatly reducing the operative risk.

(2) Complete disappearance occurred of intraperitoneal inflammatory reaction involving the jejunum, colon, their mesenteries and the adjacent peritoneum. In two instances the ulcerations themselves disappeared.



(3) Colonic contamination was avoided and adequate protection of the repaired transverse colon was secured, thus abolishing the danger of leakage and peritonitis.

(4) The disastrous general and local results of gastrojejunocolic fistula are in large part due to reflux from the colon into the upper digestive tract and not from loss of gastric contents into the colon, as hitherto suggested.

(5) Preliminary colostomy is indicated before attempts to carry out the formidable procedures necessary to correct gastrojejunocolic fistula.

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DISCUSSION.—DR. FREDERICK A. COLLIER (Ann Arbor, Mich.): Gastrojejunocolic fistulae are notoriously unsatisfactory to treat, and I am sure Doctor Pfeiffer has made a real contribution in the procedure that he has described this morning. As he stated, the operative mortality is high; patients may die from shock because the operation is a prolonged one, on undernourished patients. Postoperative pulmonary complications are common, and of course peritonitis is an ever present danger, and a very frequent complication and cause of death, because one is working with three organs that contain colonic contents.

Two years ago, Dr. Arthur Allen advised and described a method for aseptic resection of this lesion, and I have employed it with satisfaction in the smaller lesions. However, I have found that I, at least, cannot use it in some of the larger lesions such as those described by Doctor Pfeiffer, and I believe that his procedure has a real place as a preliminary to the aseptic method which can be employed at a later date.

There is another factor, however, that I think one should stress here. You cannot find a patient with a higher degree of malnutrition than these people present. In the first place, they cannot eat, or they will not eat, because they have the ulcer; and in the second place, if they do eat, their gastro-intestinal tract is very efficaciously short-circuited in many cases and the food cannot go where it will be utilized.

I have found that many of them are dehydrated because they have a profuse

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diarrhea. I have encountered the most advanced cases of alkalosis that I have ever seen in this group of patients, and many of these patients have actually had clinical signs of scurvy. I believe that no group of patients deserves more careful preparation before operation than these cases. I cannot give you the exact mortality in our own patients prior to 1930, but it was high, probably about 40 per cent.

In 1930, we decided that we would spend a week or more in getting these patients ready, by transfusions and dietary regimen, high in vitamins, *etc.* Since that time we have operated upon 14 patients with gastrojejunocolic fistulae. In 1931, the first patient that we operated upon after we decided to spend this time in getting them ready died on the eighteenth day of a lung abscess. Our next patient died of peritonitis because of a leak from the anastomosis in the colon, but since that time we have had 12 patients upon whom we have carried out one-stage operations; all of them have recovered, I think largely due to the fact that we had prepared them very, very carefully, corrected their chemical abnormalities, brought their blood to normal, and taken plenty of time to do this before the operation was undertaken.

Every one of these patients presented lesions secondary to gastroenterostomy for duodenal ulcer. We try to restore the gastro-intestinal tract to normal, and we have done that in all of these patients that I mentioned. In three instances, the pylorus was closed by scar and we had to perform, in addition to the closure of the three involved organs, a pyloroplasty. All of them have done well except two, who have had a reactivation of their original duodenal ulcer. One of these was relieved by medical management, and I was obliged to perform a high resection of the stomach in the other.

I think if one will take plenty of time to prepare them and then utilize the operative principles of Allen and Pfeiffer, the results should be very much better.

DR. CARL EGGERS (New York): About 12 years ago, a patient with an established diagnosis of gastrojejunocolic fistula came under my care. The symptoms were distressing. He complained chiefly of diarrhea, having to defecate as often as 12 times a day. As a result of this, emaciation was the outstanding manifestation. He weighed only 90 pounds. There were no ulcer symptoms. It appeared to us that closure of the communication with the colon was of the greatest importance. We realized that the patient would not be able to stand a prolonged operative procedure such as is required for separation of the stomach and intestine, with possible subsequent resection.

We therefore devised a method of less magnitude. Reasoning that the part of the colon which was attached to the stomach had become accustomed to receive acid gastric contents and would probably be able to protect itself against it in the future, we therefore divided the transverse colon proximal and distal to the fistula. After closing both ends, we left the midportion of the transverse colon as a permanent part of the stomach. The proximal and distal colon were united with an end-to-end suture, thus reestablishing normal continuity. The result was very satisfactory.

Some years later, however, the patient had recurrence of ulcer at the site of his original lesion in the duodenum with acute perforation. This was closed by suture.

Two years ago, he was admitted with acute intestinal obstruction due to carcinoma of the ascending colon. This was successfully resected.

DR. FRANK H. LAHEY (Boston): It is obvious that this lesion, gastrojejunocolic fistula, has been a difficult one for us all to deal with. I think I should present our experience and the plan I recently devised to manage it, although it may not be the best one. None of us has had enough experience

with the newer developments in the management of these plans to really know yet which is the best one. I would like to discuss a plan which we have employed in two cases. Dr. I. J. Walker, of Boston, who asked my advice concerning the management of such a lesion, has also successfully employed this procedure in a similar case of gastrojejunal fistula.

The thing that has bothered us in the management of the gastrojejunal ulcer is the peritoneal contamination which results from detaching the fistula into the colon. We have for some time sought for a plan to avoid opening the fistulous tract, but to permit resection of the stomach and jejunum. In these two cases the ileum as a preliminary measure has been cut across, the distal end closed and the proximal end implanted into the descending colon as a first-stage of the procedure. Then, at the end of two weeks, the ascending colon, the remaining terminal ileum, the fistula, the jejunum and the portion of the stomach to be resected are taken out in one block, and the end of the transverse colon distal to the fistula closed with the fecal stream already established.

This has been a very satisfactory method of handling this problem to avoid contamination, and although it sounds like an operation of tremendous magnitude, the colon is mobilized readily and it is not as difficult to perform as it seems.

DR. DAMON B. PFEIFFER (closing): I appreciate these discussions and the additional value of the experience and suggestions made. I realize that the subject is not fully and finally settled by my observations, but it seems an inescapable conclusion that the three clinical observations here recorded throw a new light on the mechanism of the production of symptoms resulting from gastrojejunal fistula, and that a simple and safe method of rehabilitation is offered. The idea that the loss of health is due largely to escape of gastric contents directly into the colon seems untenable, because, in the first case, there was no such loss, as has been demonstrated roentgenologically, and to the failure of the food to pass into the colon after colostomy. In the second place, moreover, although some gastric contents did find their way directly through the fistula into the colon, it was found that after colostomy the same favorable effects occurred even though there was some continued passage of food into the colon. Although the bulk of the gastric contents passed into the small intestine, the same alleviation of gastric and colonic symptoms was noted. The third case bears out the same point. All this indicates that the disastrous effects of this type of fistula are due to passage of colonic contents into the upper gastrointestinal tract rather than the reverse. Exclusion is, therefore, the sound and simple method of bringing these cases back into a state in which the necessary complicated surgery may be accomplished with relative safety. It seems probable that resection, or resection by exclusion, may be the accepted method of dealing with these ulcer ridden cases, and after complete rehabilitation this is not too dangerous a procedure.

I am lost in admiration of Doctor Collier's last series of 11 cases without a death. Doubtless with the newer methods of handling nutrition and fluid and chemical balance much can be accomplished without colostomy. It has not been our experience, however, even with the most strenuous efforts under hospitalization, that we have been able to improve the patient's condition to a satisfactory degree. Even if this can be accomplished, it would seem that the increased danger of performing radical surgery upon an area teeming with the bacterial flora of the colon must be greater than when this factor is eliminated. Certainly in cases which cannot be well controlled, the plan advocated will be found of value.

## SCLEROSING OR RETRACTILE MESENTERITIS\*†

ITS TREATMENT AND THAT OF ADHESIONS WITH THE ELECTROSURGICAL KNIFE

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THICKENING and shortening of the mesentery, with great distention of the lymphatics in the involved mesentery and bowel, were observed when we ligated in continuity all the vessels, artery, vein and lymphatics, to a small segment of bowel. The same result occurred when the lymphatics to the segment were ligated. The ligations were made in the region of the second and third branching. The bowel itself showed very little alteration except possibly a little thickening.

This retraction and thickening of the mesentery reminded us of certain clinical cases, infrequently seen, in which certain areas of the mesentery were found thickened and retracted.

In the paper by Reichert and Mathes<sup>1</sup> on experimental lymphedema of the intestinal tract and its relation to regional cicatrizing enteritis, Case 3 (M. P.) was that of a man who had suffered a severe blow on the abdomen from the steering wheel of an automobile. He was operated upon two months later for intestinal obstruction. An area of ileum was found bound down and kinked. The mesentery was very short, boggy and thick. At one point in its root, a small mass of dark colored material, either fecal matter or old, unabsorbed blood pigment, was found. Resection of the involved bowel and mesentery cured the condition. The pathologic study of the resected ileum showed chronic ileitis with the submucosa greatly thickened and edematous. The lacteals between the muscular layers were greatly engorged and many were thrombosed.

Another patient (M. H.), a boy, age 14, two years before entry had had acute appendicitis with possible rupture. Appendicectomy with drainage was performed at another hospital. He remained well until two months before admission, when his first and only attack of cramps, in the right lower quadrant, and soreness developed. Hot stupes and manipulation of the abdominal wall with the patient in the knee-chest position relieved the pain. A diagnosis of intra-abdominal adhesions was made. At operation omental adhesions to the cecum and terminal ileum were freed with the electrosurgical knife. A fibrous band, 3 Mm. thick and 4 cm. long, extending from ileac wall to terminal ileac wall, so arched the bowel that a loop of intestine could easily slip between and cause obstruction. The terminal ileum was narrowed and angulated by fibrous contracture of the mesentery. The regions with narrowing, angulation and

\* Aided by a grant from the Fluid Research Fund of the Rockefeller Foundation.

† Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

contracture were released by lightly coagulating the scar tissue and letting it pull apart. The bowel wall was somewhat thickened, probably from the scarring and retraction of the mesentery with lymphatic block, rather than being a true regional ileitis.

We reviewed the work of Welch and Mall<sup>2</sup> on hemorrhagic infarction but could find only an occasional mention of the lymphatics and none of mesenteric retraction among their many beautiful experiments.

Our search in the modern text-books of surgery revealed no mention of retractile mesenteritis, *per se*, although great thickening of the mesentery was discussed under the recently described condition of regional enteritis.

In Volume 4 of Keen's System of Surgery, 1908, Van Hook and Kanavel describe contraction of the mesentery and quote the observations of O. Brehm,<sup>3</sup> who felt that mesenteric shrinking was not only to be regarded as an etiologic factor in volvulus of the sigmoid but also as a disease, *sui generis*, which demanded treatment. He felt that simple detorsion of angulated loops did not suffice in mesenteric contraction and that radical resection was necessary.

A number of papers on retractile mesenteritis have appeared in foreign literature during the past ten years. In Bonorino's article<sup>4</sup> on sclerotic and retractile mesenteritis he gave credit to Virchow<sup>5</sup> for describing scirrhotic mesenteritis of the sigmoid flexure, in 1853. Virchow believed that a circumscribed peritonitis with cellulitis and sclerosing degeneration in the mesentery caused its retraction, this retraction being necessary in the production of volvulus of the pelvic colon.

Subsequent to the appearance of Virchow's paper, authors have reported one or more cases of retractile mesenteritis. Tuberculosis by some, trauma by others, was considered to be the causal agent. In reviewing the case reports in the literature and those collected by Bonorino up to the year 1929, we did not feel that the descriptions were entirely similar to the condition now considered as regional enteritis.

Apparently the first experimental work on retractile mesenteritis was reported in 1927 by Jura<sup>6</sup> who, by injecting bacteria from the intestinal flora into the mesentery of the ileum, produced a lymphangitis and subsequent retractile mesenteritis.

Stropeni,<sup>7</sup> in 1933, from experiments on dogs, stated that when the mesenteric veins were ligated or injected, mesenteritis developed. He did not find any disturbance when the artery was ligated. No animals showed any infiltration of lymphatics and he concluded that trauma produced mesenteritis by interference with veins.

Milone and Picco,<sup>8,9</sup> in a preliminary note in 1933, and a complete report in 1935, discussed in detail the many and varied theories in the literature as to the etiology of retractile mesenteritis. They believed that disturbance of lymphatics caused retraction of the mesentery because absorption from the intestines was greater in lymphatics than in veins, and lymphatics were more



readily disturbed. In their experiments on rabbits they tied off the lymphatic trunks at the root of the mesentery without injuring the arteries and veins. Histologic study, one to 60 days after operation, showed that retractile mesenteritis did not develop until about the tenth day, and that the changes produced by blocking lymphatics passed through the following three stages: Diffuse edema of the mesentery with mobilization of migratory elements, especially the histocytes, first occurred. This was followed by hyperplasia of the connective tissue from new fibroblastic proliferation—at first fibrillary, then circumscribed in bundles and bands perpendicular to the direction of the lymphatics. The third stage consisted of sclerosing of newly formed connective tissue bundles and cords with gradual replacement by collagen fibers and eventual retraction of the mesentery. They concluded that the cause of mesenteritis was of intestinal origin; that it was linked with the intestinal substances or attenuated organisms of undetermined nature which penetrated the intestine through the veins or lymphatics, or were held in them in a relatively higher concentration by obstacles causing obstruction, such as hematoma after trauma, inflammation or neoplasm.

Thus in the experimental work of Jura, Stropeni, and Milone and Picco, retractile mesenteritis was produced by mesenteric inflammation from bacteria, or from ligating mesenteric veins or lymphatics. It was not produced by ligation of the mesenteric artery.

This previous experimental work on mesenteritis seemed inconclusive since the components of the circulatory system in the mesentery had not been studied in the same animal individually and collectively. From our earlier work on lymphedema<sup>1</sup> we knew of the fibrosis and scarring that developed when the lymphatic system was blocked in the bowel and in the mesentery, but we did not emphasize this finding since small amounts of the sclerosing solution leaking into the mesentery from the punctured lymphatics might have been a factor in causing the retraction.

*Experimental Investigation.*—The experiments we are now reporting concern circulatory imbalance in the canine mesentery. They can be divided into seven parts, namely, the effect produced by (1) ligating all structures, artery, vein, nerve and lymphatics, in a segment of the mesentery proximal or distal to the second branching from the root of the mesentery; (2) ligation at this level of the artery and vein; (3) ligation at this level of the lymphatics; (4) ligation at this level of the artery; (5) ligation at this level of the vein; (6) the formation at this level of hematoma in the mesentery; and (7) trauma to the mesentery.

Early in the experimentation it was realized that a number of factors must be controlled if the results were to be interpreted as being due only to the experimental procedure. Study of the protocols of the first two animals showed the necessity of assistance during the operation and of the utmost care in handling the bowel. Perhaps the greatest factor to interfere with the estimation of results was adhesions which developed when small amounts of

blood soiled the abdominal contents, or when all the talc on the gloves had not been washed off. Adhesions also developed after frequent sponging with moist gauze or when drying of the exposed bowel and mesentery occurred. As the investigation progressed it became evident that the proper treatment of adhesions was another interesting problem which will be discussed later. Photographs were taken at the operating table when reopening the animals for observations, since the alterations could not be seen well in the sacrificed animal. But the photography had to be abandoned as the drying of the exposed bowel by photo-flood lamps produced adhesions.

A summary of the experiments is given in Table I. In a single animal three to eight different ligations have been performed at stated points in the mesentery of the small bowel. Between ligations normal or control segments of mesentery intervened. When no alteration in the mesentery was found at exploration, one to eight weeks later it was indicated as o in the table. Shortening and thickening of the mesentery was indicated as + in the table.

It will not be necessary to give the protocols of each animal, but that of Dog 11 will suffice to outline the procedure and present the findings.

TABLE I  
EXPERIMENTS ON PRODUCTION OF RETRACTILE MESENTERITIS AND ITS TREATMENT

Dog	Lym- phatics Ligated	All Vessels Ligated	Artery Ligated	Vein Ligated	Artery and Vein Ligated	Hema- toma Ligated	Hema- toma + Irrita- tion	Irrita- tion	All Vessels Ligated at Root	Remarks
1.....	+	o		+	o					
2.....	o?	o?	o?	o?						
3.....	+?	+		o						
4.....		+	o	o	o				+	
5.....	+	+	o							
6.....		+	o		o					
7.....	o	+	o							
8.....	o	+	o	o	o	o			o	
9.....	+	+	o	o	o	o			o	Electrosurgical. R. No reformation
10.....	+		+?	o	o					
11.....	+	+		o	o	o			+	
12.....		Died 10 hrs. p.o.								
13.....	?	?	?	?						Loops of bowel matted together
14.....								+		Electrosurgical. R. No reformation.
15.....								+		Electrosurgical. R. No reformation
16.....								+		
17.....	+							o		Electrosurgical. R. No reformation
18.....		+					o	o		
19.....	+	+					+			Scissors. R. More exten- sive reformation
20.....								+		Scissors. R. More exten- sive reformation
21.....								+		Scissors. R. Reformation
22.....								+		Scissors. R. Reformation

+ Shortening and thickening of segment of mesentery.

o No change.

? Adhesions obscured observations.

## RETRACTILE MESENTERITIS

**Protocol of Dog 11.**—This adult female had the following experiments started, November 7, 1938:

(1) On November 7, 1938, all vessels, artery, vein and lymphatics, proximal to the third branching of a segment of the mesentery were ligated together, in continuity, with black silk. On November 18, 1938, at exploration, retraction and thickening of the mesentery was found (Fig. 1 [I]). There were no adhesions.

(2) After leaving an adjacent normal segment of mesentery as a control, a hematoma, 2 cm. in diameter, was produced between the leaves of the mesentery at the third branching by needling the vein. On November 18, 1938, the hematoma had been absorbed and no change was found in the mesentery (Fig. 1 [II]).

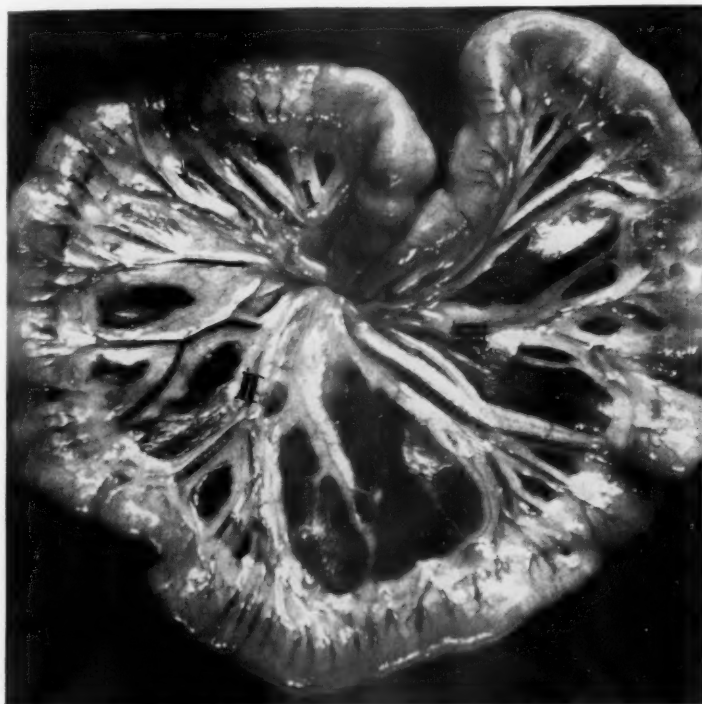


FIG. 1.—Dog 11: Photographs of ligated regions of mesentery 11 days after operation. (I) All vessels ligated in continuity producing retraction of segment of mesentery. (II) Mesenteric hematoma absorbed and no alterations in mesentery noted. (III) Artery and vein ligated but no alteration in mesentery seen.

(3) An adjacent portion of the mesentery was left for control and then the artery and vein at the third branching were ligated together in continuity. On November 18, 1938, no change was observed in the mesentery or bowel (Fig. 1 [III]).

(4) After another control segment of mesentery was left, the artery, vein and lymphatics were ligated together in continuity at the third branching. On November 18, 1938, shortening and thickening of the mesentery and slight thickening of the bowel were found (Fig. 2 [IV]).

(5) After leaving an intervening control segment of mesentery the lymphatics only were ligated in continuity at the third branching. A note was made that the accompanying artery and vein were not constricted. On November 18, 1938, slight but definite retraction of the mesentery was observed (Fig. 2 [V]).

(6) The vein was ligated at the third branching after leaving a segment of mesentery as a control. On November 18, 1938, no change was noted in the mesentery (Fig. 2 [VI]).

(7) The lymphatics only were ligated at the first branching after leaving a segment of mesentery as a control. The accompanying artery and vein were patent. On November 18, 1938, thickening and retraction of the mesentery and thickening of the bowel wall were found (Fig. 2 [VII]).

(8) A segment of mesentery was left as a control and then the artery alone was ligated at the second branching near the terminal ileum. A small hemorrhage in the mesentery occurred at the time

of ligation. On November 18, 1938, the hemorrhage had been absorbed and no alteration was noted in the mesentery. A small omental adhesion was found on the bowel near this region.

The animal was sacrificed, January 20, 1939, at which time many omental adhesions to the small bowel were found. They probably were caused by exposure and drying of the bowel and mesentery during photography.

*Summary of Experimental Results.*—The experimental findings in 22 animals may be followed in Table I.

The lymphatics in a segment of the mesentery were ligated in 11 experiments. In seven, there was definite shortening and thickening of the mesentery and one showed dilated lymphatics but no retraction.



FIG. 2.—Dog 11: Ligated regions of mesentery 11 days after operation. (IV) All vessels ligated producing retraction and thickening of the mesentery. (V) Some retraction occurred after ligation of lymphatics alone. (VI) No change seen after ligation of the vein. (VII) Retraction of mesentery and slight thickening of bowel after ligation of lymphatics at second branching.

All vessels—artery, vein and lymphatics—in a segment of the mesentery were ligated in 12 experiments. In ten, definite retraction of the mesentery occurred.

When only the artery was ligated, no retraction occurred in eight experiments. In one, a questionable shortening of the mesentery was seen beneath an omental adhesion.

When only the vein was ligated, no change in the mesentery was noted in seven experiments. In one, the mesentery was thickened and the omentum was adherent to the site of the ligation.

Hematomata were produced in the mesentery in three experiments but no retraction occurred. In two other experiments, in which a hematoma was produced and the mesentery overlying the hematoma was rubbed with gauze, one showed retraction of the mesentery. All hematomata were quickly absorbed.

When the mesentery was irritated with talc from gloves or by rubbing it with gauze, retraction occurred six times in eight such experiments. Ligation of all vessels at the root of a segment of mesentery produced retraction twice in four experiments.

We, therefore, found that retractile mesenteritis could be produced consistently when all vessels in a segment of the mesentery near the third branching were ligated. Usually, it could be obtained when the lymphatics alone were ligated or when the mesentery had been irritated or traumatized. It did not occur when the artery or the vein, or when both artery and vein, were ligated. Hematomata in the mesentery were absorbed and produced no retraction.

We agree with Milone and Picco<sup>8,9</sup> that the lymphatic stasis plays an important part in the production of retraction of the mesentery.

Careful histologic study of the mesentery and bowel in Dogs 8, 9, 17 and 19 confirmed, in general, the findings of Milone and Picco. In the later stages, that is, two or more months after ligation, we found an increase of fibroblasts and elastic tissue fibers just beneath the serosa, where they formed an irregular sheet from which long fibrous strands extended interiorly. Around some of the mesenteric vessels the van Giesson stain showed a slight increase of fibroblasts. This fibrosis, limited to the outer or superficial part of the mesentery, produced the retraction. No definite alteration was seen in the deeper areolar and fatty portion of the mesentery. In some experiments, where all vessels in a segment of mesentery were ligated, the bowel showed slight thickening, with dilation of the lacteals and edema in the musculature.

*Treatment of Retractable Mesenteritis.*—The older writers advised radical resection for retractile mesenteritis, and this seemed the only feasible procedure when the condition was extensive with angulation of the bowel, such as was found in our first case.

In our experiments, and in our second case, where the retraction was moderate and the bowel in good condition, satisfactory treatment consisted of dividing adhesions and freeing the scarred contracted mesentery with the electrosurgical knife.

Clinically, we have preferred the division of adhesions after the method of Trowbridge<sup>10</sup> who, in 1929, advised treating them with the electrosurgical knife.

In seeking proper treatment for retractile mesenteritis in animals, this method of Trowbridge's seemed to be advantageous as compared with the customary freeing of scars and adhesions with the scalpel or scissors.

Although this comparison in the treatment of retractile mesenteritis and



of adhesions was made in only eight experiments, definite conclusions could not be drawn at this time since we had not compared the two methods in the same animal.

Treatment by division with the scalpel or scissors of omental and mesenteric adhesions and of retractile mesenteritis was employed in four animals. No attempt was made to peritonize the raw surfaces. Subsequent explorations showed, in all four animals, reformation of adhesions and more retraction of the mesentery. In two, the adhesions were more extensive after this form of treatment.

Employment of the electrosurgical knife, set for slow coagulation, was used to separate and free omental and mesenteric adhesions and retractile mesenteritis in four other animals. Separation was made with ease by keeping the adherent areas under slight tension. Subsequent exploration showed that the adhesions had not reformed in the cauterized areas, and the sclerosed mesentery showed no or only slight retraction.

**Protocol of Dog 9.**—An adult female, the following are the findings after the use of the electrosurgical knife to separate adherent areas.

(1) On October 26, 1938, all vessels were ligated in continuity in a segment of the mesentery at the third branch. On November 3, 1938, the mesentery was found retracted. There were no adhesions. On December 5, 1938, the fine mesenteric scars were separated by electrocoagulation. On December 12, 1938, no adhesions and no retraction was found. On January 20, 1939, no adhesions and no retraction was seen.

(2) On October 26, 1938, the lymphatics only were ligated in a segment of mesentery. On November 3, 1938, the mesentery was found shortened and thickened with dilated lymphatics on the surface of the involved bowel. No adhesions were present. On December 5, 1938, both sides of the contracted mesentery were touched lightly with the electrosurgical knife. On December 12, 1938, and January 20, 1939, no retraction had recurred and there were no adhesions.

(3) On October 26, 1938, the artery alone was ligated at the third branching. On November 3, 1938, no changes were found. On December 5, 1938, small collateral arterial vessels had developed around the point of ligation. On December 12, 1938, and January 20, 1939, no further changes had occurred.

(4) On October 26, 1938, the vein was ligated at the third branch. On November 3, December 5, and 12, 1938, and January 20, 1939, no changes were seen.

(5) On October 26, 1938, the artery and vein were ligated together. On November 3, December 5, and 12, 1938, and January 20, 1939, no alterations were noted.

(6) On October 26, 1938, a hematoma, about 2 cm. in diameter, was produced between the third and fourth branchings. On November 3, 1938, slight infiltration and discoloration was noted. On December 5, 1938, this region appeared to be normal and continued so when observed, December 12, 1938, and January 20, 1939.

(7) On October 26, 1938, three hematomata were produced between the fourth and fifth branchings near the mesenteric attachment to the bowel. On November 3, December 5, and 12, 1938, and January 20, 1939, the area appeared to be normal.

(8) On October 26, 1938, all vessels at the second branching were ligated. On November 3, 1938, there was no retraction, but lace-like opaque areas were seen on the mesentery. On December 5, 1938, scars were divided with the electrosurgical knife. On December 12, 1938, and January 20, 1939, a slight decrease in amount of scarring was noted.

**Comments on Protocol of Dog 9.**—At the first operation extreme care was taken in handling the bowel and in keeping it moistened with warm normal saline. Gauze was applied only once to the mesentery to control oozing at the site of a hematoma. On December 5, 1938, at the third operation in the region where the fourth, fifth and sixth ligations were made, a large omental adhesion was attached to the bowel wall for a distance of three inches. This adhesion was freed from the bowel by electrocoagulation (Fig. 3). In

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FIG. 3.—Dog 9: Shows division of adhesions with electrosurgical knife.

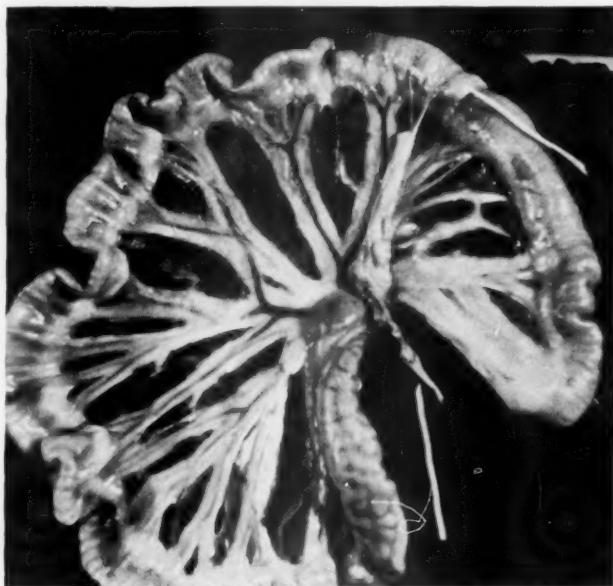


FIG. 4.—Dog 9, January 20, 1939: Upper indicator lies over normal bowel to which omentum had been adherent. Bowel freed from omentum with the electrosurgical knife one month previously. A new omental adhesion had developed to normal adjacent bowel. The lower indicator points to a free strand of omentum which had been freed from the mesentery one month before by means of the electrosurgical knife.

order to identify the areas divided, a black silk tie with ends 5 mm. long was placed on the bowel where the omentum was freed. Another similar tie was fastened to the omental stump. The same treatment and similar identification marks were applied to another small omental adhesion attached to a small area of mesentery. On December 12, 1938, at the fourth operation, the small bowel showed slight scarification of the serosa over the area freed from the omental adhesion. A pencil-like strand of omentum was attached to the black tie on the bowel. Another end of omentum had attached itself to the black tie on the mesentery where the other adhesions had been freed. This formation of adhesions to the knot area has just been described in the experiments of Donaldson and Cameron.<sup>11</sup> On January 20, 1939, the abdomen was opened and observation and photographs made. Wherever electrocoagulation had been used no adhesions were found. Where the retracted mesentery had likewise been freed, scarring was present but no retraction persisted. The only indications of electrocoagulation were several small yellowish scars in the serosa. The area of bowel to which the omentum had been adherent showed no adhesion or scarification, and is indicated in Figure 4 by the match-stick on the bowel. One new adhesion had formed near this area on normal bowel, probably from trauma and exposure. The other match-stick points to a free omental tag previously separated from the mesentery by electrocoagulation.

Although these experiments on the treatment of mild retractile mesenteritis and of adhesions are not conclusive, they at least suggest that electrosurgical division of adhesions is far superior to the customary division with scalpel or scissors. Apparently division by coagulation leaves dead tissue on the exposed surface with healing occurring beneath before separation of the scar. This would prevent new points of adhesion.

#### CONCLUSIONS

Retractile mesenteritis is no longer mentioned in the modern text-books of surgery.

Retraction of the mesentery is discussed in texts, as occurring in the recently described condition of regional enteritis.

One of our cases with retractile mesenteritis has been reported as a case of regional enteritis. The other case also might be considered as a mild instance of regional enteritis.

European investigators have reported experiments in which retractile mesenteritis was produced by mesenteric inflammation from bacteria, or by ligating mesenteric veins or lymphatics.

We found that retractile mesenteritis could be produced consistently when all vessels in a segment of the mesentery were ligated. Usually it could be developed when the lymphatics alone were ligated or when the mesenteric leaves had been irritated or traumatized.

Our experiments indicated that lymphatic stasis played an important part in the production of retraction of the mesentery, since it did not occur when the artery and vein, or each alone, were ligated.

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Since mild degrees of retractile mesenteritis were produced experimentally, radical resection was not considered as the proper treatment.

In the treatment of experimental retractile mesenteritis and intra-abdominal adhesions, the electrosurgical knife was found to be superior to the customary division with scissors or scalpel.

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DISCUSSION.—DR. JOHN HOMANS (Boston): Doctor Reichert's skill with the fine needle has led him into a field into which very few of us are able to follow. He was able experimentally, for instance, to reproduce, in a very practical way, what seems to have been a regional enteritis, and not satisfied with that, he has refined his experiment and produced chronic thickening in the mesentery by what seem to be impossibly simple means.

In that respect, it is rather interesting to speculate upon why lymphatics behave in this way, and that is my excuse for discussing this paper, for I know nothing whatever about the cicatrizing changes in the mesentery. I take it that most of us would notice them if our eyes were open to them, but apparently we have not taken much note of them.

If lymphatics are divided on a large scale, as in experiments which Doctor Reichert performed years ago, and the whole leg is encircled by an incision, they find no difficulty in crossing the scar, but apparently they are very subject to disorganization for other reasons. If, for instance, one plugs up the lymphatics over a considerable area, they appear to go to pieces and the tissues which they drain tend to become first edematous and then indurated by the formation of new tissue.

Doctor Homans then showed a drawing made from a roentgenogram, taken following the injection of lipiodol, demonstrating the veins of the dog's leg, with the lymphatics outlined in black. One could see, at a point behind the knee, a lymph node with a large number of entering vessels, and at a

point nearer the body, a place where one ought to be able to interrupt most of the large lymphatics.

A second roentgenogram was shown of an animal whose principal lymph vessels had been tied off. Perhaps ten days or a week afterward, the animal was given thoratrast in its paw, which demonstrated the lymphatics, which appeared to be quite orderly vessels of rather large size.

Apparently, with time, these obstructed vessels dilate, losing the use of their effective valves, which was demonstrated by a roentgenogram taken some four or five weeks afterward, in which one could see traces of the thoratrast and perhaps the remains of the larger vessels, as if they were dilated and had succeeded in absorbing only a very little thoratrast.

Doctor Homans took this to indicate that once the lymphatics have been interrupted and have been unable to reform, they tend to become disorganized, and perhaps that is the reason why, for anatomic reasons, of which we know very little, in certain parts of the body, possibly because of the presence of terminal vessels, quite remarkable effects can be produced by division of these vessels.

Of course the by-product of this investigation was perhaps as interesting a part of it as any, namely, that the division of adhesions by the coagulating current was a very efficient way of dealing with intraperitoneal bands.

DR. ARNOLD SCHWYZER (St. Paul, Minn.): I was impressed when I heard that simple ligation of the lymphatics in the mesentery causes retractile mesenteritis. We all have seen in cases of appendicitis in the lowest ileum loop now and then a marked retraction of the mesentery, but where is the origin of a regional ileitis or a retractile mesenteritis farther up? That could be a problem.

I saw two cases which might give a clue, and that is why I rose. The two cases, one a very recent one, were of acute appendicitis, and in both instances was found a large abscessed node at the root of the mesentery. Now, you would expect that these nodes would be located right at the ileocolic junction, but nothing of the kind. There was no direct connection between the appendix and the abscessed nodes, which in one case was in the midline above the promontory. In the second case, it was even a little to the left of the midline. I suppose that the whole area of lymphatics was affected and over the lumbar vertebrae some mechanical damage was added, which caused a breaking down of a node with abscess formation.

In this way, one can think that even farther up on the ileum an appendiceal infection may be the primary cause of a regional ileitis and retractile mesenteritis.

DR. MARTIN B. TINKER (Ithaca, N. Y.): I would like to discuss electrosurgery in abdominal cases. There must be several here who attended the symposium at the College of Surgeons in Philadelphia some five or six years ago, at which the question of electrosurgery was discussed and its advantages were brought forward. It seems that the men who have profited most by using electrosurgery have been interested in neurologic surgery, and who, with Cushing's lead, have used it very extensively.

I have been impressed, however, with its value in abdominal conditions, such as Doctor Reichert mentioned. Three patients who came in with recurrent intestinal obstruction had been operated upon two and three times before, without permanent results, the obstruction recurring. It seemed that the more favorable results following electrosurgery in freeing adhesions in these cases was the factor that gave permanent results. In several cases they have remained well two and three years following operation, or longer, where



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recurrence had followed promptly previously. Doctor Reichert's experimental studies confirm and explain clinical experience.

DR. JOHN A. WOLFER (Chicago): I believe we all recognize that the lymphatic system, especially as it exists in the mesentery of the bowel, is a very complex one. I believe it has been proven by a number of men that if dyes or opaque materials are injected into a segment of bowel or its mesentery, and the lymphatics in the immediate zone are obstructed, that the opaque materials take a rather circuitous route and eventually arrive in the main lymphatic channels or nodes proximal to the site of obstruction. I am wondering if the fact that there is a very rich collateral lymphatic circulation in the mesentery was taken into consideration in arriving at conclusions.

DR. F. L. REICHERT (San Francisco): I wish to thank the members for their discussion and to answer Doctor Wolfer's question. The amount of bowel involved in a ligation usually was between two and three inches, and from our previous work we felt that this degree of involvement took in all of the lymphatics of that part. Of course there is anastomosis on either side. That also developed when we ligated all of the structures in that region.

## LIVER TRAUMA AND THE HEPATORENAL SYNDROME\*

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THE IMPORTANCE of the toxic effect of liver trauma upon the kidneys was first emphasized by F. C. Helwig and his associates.<sup>1, 2, 3</sup> At the time of their studies in 1932, a case was reported in which the important observations of interest were a traumatic necrosis of the liver with extensive retention of creatinine, and a high grade nephrosis. The patient was a boy, age 15, who had received a severe automobile injury. He died 11 days following the accident. His principal clinical symptoms were a temperature of 102.8° F., vomiting, secondary anemia, leukocytosis, jaundice, almost complete suppression of urine, generalized edema, moderate abdominal distention, and red blood cells and albumin in the urine. The nonprotein nitrogen was 240 mg. and the creatinine 25 mg. per 100 cc. of blood before death. Operation on the sixth day revealed a large quantity of bloody, bile-stained fluid in the abdomen. An autopsy showed a large area of pulpified liver tissue in the right lobe, large swollen kidneys, blood- and bile-stained ascitic fluid, bloody fluid in the pleural cavities, parenchymatous and subpleural hemorrhages in the lung, and subserous and submucous hemorrhages in the large intestine. Microscopically, the damaged liver showed extensive necrosis. The pathologic changes observed in the kidneys were leukocytic infiltration in the medullary portion, interstitial hemorrhages, dilated small vessels, red cells in the tubules of the medulla, cloudy swelling, albuminous precipitate and pale casts in the collecting tubules, parenchymatous degeneration in the convoluted tubules and loops of Henle, swelling of the glomerular epithelium with red cells between the tuft and capsule, and polymorphonuclear leukocytes in the capillary channels.

At the time of the above report, only one case of liver trauma was found recorded in the literature, which had been carefully studied from the standpoint of its relation to kidney damage. Furtwaengler<sup>4</sup> reported this case in 1927, from Professor Clairmont's Clinic in Zurich. He described a diffuse cortical necrosis of both kidneys following a severe injury to the liver, which resulted in death in three days. He recognized the relationship between liver damage and renal necrosis and explained the latter on the basis of an ischemia produced by a chemical toxin liberated in the blood stream as a result of decomposition of hepatic tissue. He believed that vascular spasm followed by ischemia produced the renal necrosis. Henschen<sup>5</sup> mentions that Volkman-Münster has seen a case of gunshot wound of the liver and that he has observed a case of liver rupture, both of which died of lipoid degeneration of the kidneys.

\* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

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In 1930, McKnight<sup>6</sup> reported a case of severe liver trauma which had a blood urea as high as 268 mg. per 100 cc. of blood. The urine on admission was entirely normal but at various times later showed sugar, albumin, and hyaline and granular casts. He considered the high blood urea as evidence of gastrointestinal stasis and mentioned that it might have been associated with renal impairment. In 1930, Stanton<sup>7</sup> also recorded the case of a young man who died 47 hours after a traumatic rupture of the liver with a temperature which reached 105.6° F. in 22 hours after the accident. He remarks that this case presented a clinical picture similar to that seen in the rapid deaths following gallbladder operations and was inclined to believe that similar factors were operative in his case. No blood studies were made and no pathologic changes in the kidneys were mentioned. In 1934, Rosenbaum<sup>8</sup> observed a patient with lethal anuria following liver rupture. His patient was a male, age 65, who died 30 hours following an accident. Extensive epithelial degeneration was found in the collecting tubules of the kidneys. Death was attributed to nephrosis with anuria. Helwig and Schutz<sup>9</sup> added another case report in 1935. The patient was a male, age 61, who had been injured in an automobile accident. His principal signs and symptoms were pain in the right chest, a temperature which ranged from 99° to 102° F., tenderness over the right ribs and right abdomen, abdominal distention, slight edema, diminished urinary output, and albumin, hyaline casts, and red blood cells in the urine. On admission to the hospital soon after the injury, the urine, blood, and blood chemistry were normal. The third day after the accident the blood nonprotein nitrogen was 75 mg. and the creatinine 3 mg. per 100 cc. At autopsy extensive laceration of the liver with some pulpefaction was found. The liver cells showed varying stages of necrosis and disintegration. Cloudy swelling, vacuolar degeneration, and loss of nuclei of the tubular epithelium were the outstanding histologic changes in the kidneys. In a general discussion of "liver death" in 1935, Boyce and McFetridge<sup>10</sup> recorded three cases of gunshot wound of the liver and one case of liver injury due to automobile accident in which the temperature reached 105.4° to 108.2° F. These patients all died, but no pathologic studies were made. Two other cases of severe liver injury following automobile accidents revealed at autopsy typical degenerative changes in both liver and kidneys. In one of these cases the jaundice was quite marked with an icteric index of 210. Becker<sup>11</sup> reports a case from Henschen's Clinic in Basel. His patient was a male, age 27, who had been injured in an automobile accident. The patient died six hours following operation, in less than 24 hours following the injury. A large laceration was found in the right lobe of the liver. Microscopic examination of the kidneys showed parenchymatous degeneration of the cortex and necrosis of the epithelium of the convoluted tubules. He attributed these changes to a pathologic relationship between the damaged liver and the kidneys. Blood studies were not recorded.

Five cases of liver injury associated with kidney damage are reported herewith. Four cases were studied in the University of Kansas Hospitals, Kansas City, Kansas, and one in St. Luke's Hospital, Kansas City, Missouri.

## CASE REPORTS

**Case 1.**—E. T., white, male, age 17, was injured in an automobile accident, December 18, 1932. He was admitted to the hospital at once, in a mild state of shock with tenderness and rigidity of the right upper abdominal muscles. Three hours after the accident he was operated upon and a deep laceration was found in the inferior surface of the right lobe of the liver. There was a large quantity of blood in the abdomen. The wound in the liver was packed with gauze and the abdomen drained. With multiple transfusions his condition improved. He was delirious for three days. A *Streptococcus hemolyticus* infection developed in his wound which delayed recovery. At the end of four weeks an empyema was drained which showed a culture of *Staphylococcus aureus* and *Staphylococcus hemolyticus*. During the height of his infection his fever reached 104° F. He recovered and was discharged from the hospital at the end of three months.

The urine contained albumin and pus cells. Blood chemical studies on the day following the injury showed a nonprotein nitrogen of 82 mg. and creatinine of 4 mg. per 100 cc. These changes returned to normal on the fourth postoperative day (Table I). The second day following the accident the icteric index was 10.

**Case 2.**—T. J., male, age seven, was struck by an automobile, May 16, 1933. He was brought immediately to the hospital in a profound state of shock. There were abrasions on the right abdominal wall, forehead and leg. Some blood cells were found in the urine. His general condition improved with transfusions and infusions. Restlessness and delirium were marked symptoms throughout his illness. An abdominal exploration was made 24 hours after the accident. The abdomen was filled with blood. A deep laceration was found extending far back into the inferior portion of the right lobe of the liver. There was some retroperitoneal hemorrhage about the right kidney. Bleeding from the liver was controlled with a gauze pack. The highest temperature recorded during the first three days was 105.4° F. A slight cyanosis developed and oxygen therapy was given. Infection developed in the wound which showed a *Staphylococcus aureus* and a nonhemolytic *Streptococcus*. During the course of the illness blood cells in the urine decreased and coarsely granular casts and occasionally a few pus cells appeared. Granular casts were found in the urine throughout the illness. The blood count showed a leukocytosis and secondary anemia. The day after injury the nonprotein nitrogen reached 131 mg. and the creatinine 4.1 mg. per 100 cc. of blood. Changes in blood chemistry returned to normal on the sixth day of the illness (Table I). Death occurred on the eleventh day following the injury. Autopsy showed an irregular laceration 12 cm. long in the superior portion of the right lobe of the liver extending through to the inferior surface. There were also infarction and early pulpification of the liver, thrombosis of the renal veins with infarction of the right kidney, compensatory hypertrophy of the right kidney, perirenal hemorrhage, hemopericardium, acute serofibrinous pleurisy, atelectasis of the lungs and acute generalized peritonitis.

Pathologic histology of the injured area of the liver revealed marked necrosis, vacuolization of liver cells, edema, infiltration with polymorphonuclear and mononuclear leukocytes, proliferating bile ducts and organizing exudate on the surface. The changes in the kidneys were cloudy swelling distention of convoluted tubules, congestion of glomerular tufts, hemorrhages in the medulla, hyaline casts in the tubules, edema, atrophy of some of the convoluted tubules, some infiltration with mononuclear leukocytes, occasional polymorphonuclear leukocytes in the collecting tubules, coagulation necrosis in the infarcted area of the kidney, and thrombi in the renal veins.

**Case 3.**—R. V. H., white, male, age 23, was injured, June 27, 1933, by being thrown from a truck. He was admitted to the hospital within two hours, in a state of shock. Examination revealed a fractured rib, subcutaneous emphysema, abrasions of the right leg, and tenderness and rigidity over the right upper abdomen. Blood was found in the urine. Roentgenograms showed partial collapse of the right lung. Two transfusions were given and at the end of nine hours after the injury the abdomen was explored. The

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TABLE I

BLOOD CHEMICAL STUDIES IN FIVE CASES OF HEPATIC TRAUMA

Case No.	Day after Injury	Nonprotein Nitrogen Mg. per 100 Cc. of Blood	Creatinine Mg. per 100 Cc. of Blood	Sugar Mg. per 100 Cc. of Blood	Carbon Dioxide Combining Power. Volume Per Cent	Whole Blood Chlorides	Remarks
1	1	82.5	4.0	100	41	490	Operation 3 hrs. after injury. First blood study 36 hrs. after injury. Recovery
	2	79.8	2.0	77	43	490	
	3	68.3	1.9	99	33	550	
	4	34.0	1.5	153	46	580	
	5		1.5	83		500	
2	0 A.M.	68	2.1	101		550	Operation 24 hrs. after injury. First blood study 15 hrs. after injury. Death
	0 P.M.	58	2.3	132		520	
	1	131	4.1				
	2 A.M.	98	3.3	118		560	
	2 P.M.	62	2.7				
	3	71	2.8	145	33	590	
	4	53	1.9	100	39	550	
	6	44	1.7				
3		37			37		Operation 9 hrs. after injury. First blood study within 24 hrs. after injury. Recovery
	0	45	2.2	133			
	1	65	2.3	142	44	530	
	2 A.M.	57	2.0	127	36	510	
	2 P.M.	67	2.0	125		540	
	3	73	2.0	133		525	
	4	42	1.5				
	5	34	1.4		47	530	
4		30	1.4			610	No operation. Blood study within 12 hrs. Death
	1	85.7	2.3	93		50	
5	7	100.0	4.5	125		400	No operation. First blood study 7 days after injury. Recovery. Final blood studies 9 days after leaving the hospital
	8	93.8	5.2	105		390	
	9	100.0	4.5	95		390	
	10	100.0	6.2				
	11	79.0	4.5	118		450	
	12	86.0	3.0				
	13	60.0	3.5	102		560	
	14	60.0	3.2				
	15	60.0	3.5				
	16	58.0	2.5				
	17	49.2	2.1				
	18	54.0	2.0				
	27	26.0	1.5	62		495	



abdominal cavity contained a large quantity of blood. The round ligament was completely torn from the abdominal wall and there was a deep laceration far back into the inferior surface of the liver extending toward the hilum. Hemorrhage had almost ceased. There was some blood in the retroperitoneal tissues about the right kidney. The wound in the liver was packed with gauze. Following the operation the patient was quite ill for five days. Restlessness and delirium were sufficiently pronounced to require restraint. After the sixth postoperative day improvement was rapid. He made an uneventful recovery with the exception of a mild wound infection. The highest temperature during the first three days was 104.2° F.

The blood found in the urine on admission disappeared in two days, and granular casts were found at later examinations. Blood counts showed a leukocytosis and secondary anemia. There was a slight increase in the blood nonprotein nitrogen and creatinine the afternoon of the day of admission. In 24 hours after the injury the nonprotein nitrogen was 65 mg. and the creatinine 2.3 mg. per 100 cc. of blood. The changes in the blood chemistry returned to normal in five days (Table I).

**Case 4.**—P. H., male, age 10, was brought immediately to the hospital after having been injured by the wheel of a truck passing over his abdomen. He was in extreme shock. There were abrasions over the four lower ribs on the right and over the upper right lumbar area. The abdomen was rigid and tender. He was given a transfusion followed by infusion of dextrose in saline solution. The following morning his hemoglobin was 66 per cent and he was given another transfusion. Some dullness was noted in the flanks. A roentgenogram showed cloudiness at the base of both lungs. He vomited several times. A small quantity of blood was noted in the vomitus. Six hours after the injury he was quite irrational with a rising temperature which reached 104.2° F. before death, 17 hours after the accident. Just before death he had a convulsion. The urine showed pus cells and hyaline and granular casts. Twelve hours after the injury the nonprotein nitrogen was 85 mg. and the creatinine, 2.3 mg. per 100 cc. of blood (Table I).

At autopsy there were found a deep laceration in the dome of the right lobe of the liver, laceration of the spleen, blood in the abdominal cavity, retroperitoneal hemorrhage, pulmonary hemorrhage and edema and hemorrhage into the right adrenal. An area of liver tissue was macerated and grayish brown in color. Microscopic study of the liver showed diffuse necrosis of the injured portion with some inflammatory reaction. There were cloudy swelling of the kidneys and vacuolar hydropic changes in the cells of the convoluted tubules. The glomeruli were normal. There was some congestion of the stroma.

**Case 5.**—A male, age 49, was admitted to St. Luke's Hospital, Kansas City, Missouri, June 22, 1936, on the service of Dr. E. L. Miller. He had been kicked over the liver by a man, seven days before admission. Pain in the abdomen was immediate and grew worse gradually until he called a physician on the seventh day, when he was sent to the hospital. His general appearance indicated dehydration. Examination revealed general abdominal tenderness which was more marked in the right upper quadrant. His hemoglobin on admission was 84 per cent and the following day was 81 per cent. Some abdominal distention had developed but no evidence of blood in the peritoneal cavity was demonstrated. Operation for ruptured liver was considered but because of his generally good condition this was deferred. With sedatives and parenteral liquids he showed gradual improvement and was discharged from the hospital in 12 days without operation. The highest temperature was 99° F. The urine showed albumin, occasional hyaline casts, and a few red blood cells and pus cells for six days following admission to the hospital. When he entered the hospital the nonprotein nitrogen was 100 mg. and the creatinine 4.5 mg. per 100 cc. of blood. The changes in the blood chemistry persisted with slight increase in the creatinine to 6.2 mg. for four days and gradually decreased to 54 mg. of nonprotein nitrogen and 2 mg. of creatinine the day of discharge from the hospital, 12 days after the accident. Twenty-one days after the injury the blood chemistry was normal (Table I).

## THE HEPATORENAL SYNDROME

*Results of Experimentation.*—As soon as a relationship between liver injury and renal disease was noted, experiments were planned to reproduce the condition in animals. Helwig and Schutz attempted to traumatize the livers of dogs without breaking the liver capsule. They found it quite difficult to produce pulpefaction of the liver similar to that observed in patients. Dogs used for this work died quickly of shock after liver trauma. In dogs dying within 12 hours, they found an increase in the nitrogenous products of the blood and albumin, casts and red blood cells in the urine. The high levels in the blood nitrogen noted in clinical cases were not found. Animals living several days showed a progressive oliguria. Necropsy of animals dying within 12 hours showed parenchymatous degeneration of the more highly differentiated tubular epithelium of the kidneys and a marked hemorrhagic necrosis of the liver. They believed that their experimental results were sufficiently definite to substantiate the theory that some potent poison is elaborated by necrotic liver tissue which has a specific effect upon the kidney parenchyma. These authors were also able to demonstrate similar changes in the urine and blood after temporary ligation of the hepatic artery in rabbits. They have presented their clinical, pathologic, and experimental observations as a definite "liver-kidney syndrome."

Boyce and McFetridge attempted to reproduce the "hepatorenal syndrome" in animals by traumatizing the liver, and experienced the same difficulty as Helwig and Schutz. The changes found in the blood and urine confirmed the findings of the latter authors. Similar results were obtained by Pytel<sup>12</sup> in a series of experiments on 58 rabbits. He pointed out that there is a phylogenetic, anatomicophysilogic and pathologic relationship between the liver and kidneys. He concluded that injury and disturbance of liver circulation produced a symptom complex in animals analogous to the hepatorenal syndrome observed in man. Liver trauma was produced in a series of white rats and rabbits by Adler.<sup>13</sup> His animals developed oliguria and anuria. An increase in the rest nitrogen was observed in the rabbits. The kidney changes noted were cloudy swelling and vacuolization of the tubular epithelium. Fat droplets were demonstrable with sudan stain. Small groups of round cells were seen about dilated blood vessels. He was able to prevent the anuria and increase in rest nitrogen in rabbits by injecting "perhepar."

*DISCUSSION.*—The relationship between liver and kidney damage incident to gall tract disease has been many times recognized in cases of suspected liver death following operations. It is probable that the same syndrome occurs in other diseases, especially those within the abdomen. In a recent (1939) review of the hepatorenal syndrome, Wilensky<sup>14</sup> recognized a wide variety of hepatorenal symptoms and/or lesions including those due to chemical poisoning, abnormal physiologic states, infections, and disturbances of the ductless glands. A similar relationship exists between a traumatized liver and the kidneys. It has been generally believed that the liver, when severely injured by disease or trauma, produces a soluble toxin which causes definite pathologic changes in the kidneys. Boyce and McFetridge doubt the specificity of this

toxin but consider that the kidneys suffer in the fulfillment of the abnormal duty placed upon them. They recognize the possible direct effect of the toxin on the kidney tissue.

The five cases of liver trauma described here all manifested some degree of toxic effect upon the kidneys as shown by an increase in the blood of the non-protein nitrogen and creatinine and albumin, pus and casts in the urine. In the two cases examined at autopsy, changes similar to those already reported were observed in the liver and kidneys. It is interesting to note the rapidity with which the changes in the blood and urine occurred after severe liver injury. In less than 24 hours a retention of nitrogen was present and albumin, casts, frequently pus and erythrocytes appeared in the urine. Helwig and Schutz observed these rapid changes in the blood and urine of dogs dying within 12 hours after the liver was traumatized.

It is difficult to believe that infection is a factor in the liver and kidney changes. The three patients operated upon all had infected wounds, but the changes noted in the blood and urine were present before the infection developed. In Case 2, a general peritonitis was found at autopsy but the changes in the blood chemistry had returned to normal before death. It is believed that the cause of death in this patient was not due directly to the toxic effect of the liver trauma but to the complicating infection. In Case 1, the changes in the blood returned to normal although the patient developed a severely infected wound and later an empyema from which he recovered. In Krieg's<sup>15</sup> analysis of 60 cases of hepatic trauma, he concluded that the evidence pointed to a toxic condition on an uninfected basis. Blood and urine studies were not reported by Krieg.

From the clinician's standpoint the practical value of the blood and urine findings incident to liver trauma are worthy of consideration. Although the nitrogen retention in the blood develops early following liver damage, the importance of early operation to control hemorrhage would negate the value of the changes in the blood and urine as a diagnostic aid in many cases. However, in those cases in which bleeding is slow and the condition of the patient warrants a few hours' delay to establish the diagnosis of liver injury, the changes in the blood and urine may be of some diagnostic value. In Case 2 of this series, operation was delayed 24 hours, during which time the nonprotein nitrogen rose to 131 mg. and the creatinine to 4.1 mg. per 100 cc. of blood. This patient had other injuries complicating the picture, but knowing that such blood changes are associated with liver damage aided in confirming the diagnosis of liver rupture. Frequent estimations of the nonprotein nitrogen and creatinine may be of definite value in the prognosis. Certainly an increase in nitrogen retention indicates an increase in toxicity. Significant changes in the blood sugar, chlorides, or carbon dioxide combining power were not found. Delirium may be an outstanding symptom as observed in four of the patients reported. After a few days a hemorrhagic tendency develops similar to that observed in patients with jaundice.

In contrast to the above reports, Branch<sup>16</sup> has recently described two

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cases of severe liver injury, one of which lost approximately one-half of the liver and the other was closed after operation with a portion of necrotic liver remaining in the abdomen. Branch states that the urine and blood chemical studies in his first case were normal. Both of these patients recovered after operation. He concludes that a considerable portion of the liver must be destroyed before the so-called "liver-kidney" syndrome will appear.

The treatment of severe liver trauma is the treatment of shock plus operation to control bleeding and administration of dextrose to maintain liver glycogen and promote diuresis. The quantity of sodium chloride given must depend to some extent upon the quantity lost by vomiting. Usually the administration of chlorides is not an important factor in treatment.

### CONCLUSIONS

All evidence presented, both clinical and experimental, leads to the conclusion that a traumatized liver may elaborate an unknown toxic substance which directly affects the kidneys producing both pathologic and functional changes.

The five cases here recorded emphasize the importance of careful blood chemical and urine studies. It is suggested that these studies are of definite prognostic value and in some cases may aid in the diagnosis of liver trauma.

These reports indicate that a consideration of the prognosis and treatment of liver trauma must not only include hemorrhage, shock, and complicating infection, but, in addition, a toxic factor produced by the damaged liver cells which directly affects the kidney parenchyma, causing an increase in the blood nonprotein nitrogen and creatinine, the appearance of albumin, casts, pus, and frequently red blood cells in the urine, and a decrease in the urinary output.

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DISCUSSION.—DR. WARREN H. COLE (Chicago): This is a very intriguing subject which Doctor Orr and Doctor Helwig have brought up; I have been much interested in it ever since their initial report, although, as Doctor Orr said, some of their points are controversial. I have become convinced that the syndrome is a definite entity. Part of their hypothesis is dependent upon the supposition that the devitalized liver tissue results in the formation of a toxic product acting directly on the kidney. The complex nature of the chemical substances making up the liver, and the fact that we have plenty of evidence that on other occasions toxins may develop in tissue during the process of its degeneration or necrosis, are points supporting their hypothesis. Moreover, we can all call to mind innumerable substances which, when given to animals, have a rather specific toxic action on the kidney.

By analogy, I wish to offer further evidence supporting this traumatic hepatorenal syndrome by comparison with a patient who had the so-called hepatic insufficiency syndrome, but of the nontraumatic type. This patient was a male, age 28, with Banti's disease, a very large spleen, jaundice, and ascites. At operation, a splenectomy was performed. The liver was found to be small and very badly scarred. The operative course for three days was very satisfactory. Then, on the fourth day, he began to become delirious and developed a fever, became nauseated, began to vomit, and a few days later coma developed. During all this time there was marked leukocytosis. At first the urine was negative, as it had been on entry, but after a few days, the N. P. N. began to rise with a maximum of about 100; in the last few days albumin and blood appeared. He died on the sixteenth postoperative day; autopsy was performed. The microscopic section of the liver showed areas of necrosis of the liver cells. This necrosis was spread throughout the entire liver section, and there was an entire disarrangement of the cellular pattern. The microscopic section of the kidney showed a marked tubular degeneration with numerous hemorrhages throughout the kidney.

Summarizing, the pathologic changes in the liver and kidney along with the progress of this patient show a marked similarity to the manifestations and pathologic findings in the traumatic cases described by Dr. Orr. If it is granted that the severe renal manifestations and pathologic changes seen in nontraumatic hepatic insufficiency, of the type illustrated in the case just cited, are a part of a hepatorenal syndrome, it would appear just as logical to consider the renal changes in Doctor Orr and Doctor Helwig's traumatic cases likewise as a part of a hepatorenal syndrome.



DR. FREDERICK A. COLLIER (Ann Arbor, Mich.): I am delighted that Doctor Orr has taken up a study of this hepatorenal syndrome, because up until the present I have remained very much unimpressed by those who have written on the subject. In fact, I have never been convinced that this entity exists. However, Doctor Orr has been right so many times that I am forced to reconsider and perhaps admit myself wrong.

There is no question about the facts. Of course, the only thing on which one might differ is an explanation of why they occur. Is there a toxin, or are there other causes that might explain this high nonprotein nitrogen and the changes in kidney and urine?

Formerly, we always blamed the kidney for all of these blood alterations that have been mentioned, but it is now known that there are many causes of extrarenal azotemia. There are at least five mechanisms that may well cause a rise in nonprotein nitrogen in the blood.

It has been shown that a drop in blood pressure will cause a marked diminution in the urine volume, which diminished directly with this fall in blood pressure until a systolic value of about 77 Mm. of mercury is reached. It is entirely conceivable that in states of surgical shock associated with disease or accident, this may play a part in diminishing urinary output and causing a nitrogen retention.

Hypochloremia and hyponatremia associated with vomiting, fistulae, diarrhea, ascites or shock may be associated with rise in blood proteids, although it has been suggested that sodium loss causes dehydration, which in turn will increase the concentration of the blood.

We rather commonly find high nonprotein nitrogen values from the blood associated with alkalosis due to pyloric obstruction and peritonitis. Dehydration will cause a concentration of the blood and all of its elements. Lashmet and Newburgh have shown that in normal conditions the kidneys excrete 35 to 40 Gm. of solids a day. This requires at least 500 to 600 cc. of urine for kidneys working at their maximal concentration. If the output is less than this, or if the kidneys have a decreased concentrating solution, there will be a nitrogen retention.

We carried out studies on healthy individuals who submitted to voluntary abstinence from water for several days, and it was found that there was a very definite rise in the nonprotein nitrogen of the blood caused by this mild type of dehydration. The urine showed very marked changes, the presence of albumin, increased casts, and red blood cells.

About three years ago, there were a number of papers published in which it was alleged that acute nephritis is frequently associated with acute cholecystitis. One observer reported eight cases with acute cholecystitis that died of acute nephritis. A typical history of one of these cases runs about as follows: A woman, admitted to the hospital in a typical attack of acute cholecystitis that had been present for three days. During this time she had not been able to eat or drink and had been vomiting. On admission to the hospital the patient was given half a liter of 50 per cent glucose and the following several days until her death, she was given about a liter of salt solution.

In comment, one may say that the patient entered the hospital dehydrated, was further dehydrated by the administration of hypertonic solution and was given inadequate fluids from then on. The urinary changes undoubtedly were entirely due to this drastic dehydration caused by disease and by treatment. This of course does not apply to the patients presented by Doctor

Orr but I relate it to show that dehydration may well produce distinctly abnormal urine.

Protein catabolism if increased is reflected by an increase in the urinary excretion of nitrogen. This occurs with large abscesses, septic inflammations such as pneumonia, peritonitis, septicemia, or even associated with severe surgical trauma. Damage to the liver itself, such as in cases of acute yellow atrophy, may cause a marked rise in the meno-acid nitrogen, and I am very inclined to believe that the damage to the liver in the cases presented by Doctor Orr may well play a part in producing the azotemia and abnormal urinary findings.

In short, it is my belief that while there may be a specific toxin generated by the injured liver that acts directly upon the kidneys, I think that in cases with liver damage we must remember that infection, fever, low blood pressure and dehydration may well be factors in causing nitrogen retention and in producing the urinary abnormalities that have been presented to us today; and certainly further studies, with these other factors in mind, must be made before we have definite proof of the existence of the hepatorenal syndrome as a clinical entity.

DR. THOMAS G. ORR (closing): I have presented these cases as they are without any effort to explain the hepatorenal syndrome. I think that Doctor Coller would be the man to explain the mechanism of these changes in the liver and the kidney. A short time ago, Wilensky reviewed a large group of conditions which he thinks produce this so-called hepatorenal syndrome. I am not prepared to accept the condition wholesale, because there are so many other factors to be taken into consideration. Lastly, I am very happy that Doctor Coller now has become hepatorenal minded.

## CONTROL OF POSTOPERATIVE BLEEDING IN OBSTRUCTIVE JAUNDICE\*

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MUCH convincing experimental and clinical evidence has been adduced during the past five years bearing on the mechanism of pathologic bleeding in obstructive jaundice.<sup>1,2,3,4</sup> Such bleeding has been shown to depend upon reduction in plasma prothrombin, which is probably part of the globulin fraction of plasma protein, formed by the liver. A fat-soluble substance, or substances, rather widely distributed in animal and vegetable fats and called vitamin K by Dam<sup>5</sup> must be absorbed from the gastro-intestinal tract in the presence of bile salts for maintenance of normal prothrombin concentration. This metabolic process may be disturbed by factors depressing liver function, by lack of bile salts in the intestine, by insufficient intake of foods containing vitamin K, and probably by too rapid movement of the intestinal stream or too little absorptive intestinal mucosa. These considerations have a direct bearing on the control of the bleeding tendency in obstructive jaundice.

The data herewith presented were obtained in the management of cases of obstructive jaundice at the Massachusetts General Hospital during the past 12 months.

*Methods Employed.*—These have been previously described.<sup>6</sup> The method of Warner, Brinkhous and Smith, with modifications as described, has proved entirely satisfactory in the determination of plasma prothrombin. Measurement of plasma prothrombin, bilirubin and fibrinogen were made at frequent intervals before and after operation. The vitamin K extract used in this work was prepared from fresh spinach according to the method of Dam, and was mixed with sodium glycocholate and sodium taurocholate and put up in gelatin capsules containing 0.2 Gm. Each gram of the mixture was composed of 0.45 Gm. sodium glycocholate, 0.45 Gm. sodium taurocholate, and 0.1 Gm. of vitamin K extract derived from 200 Gm. of fresh spinach. The same lot of vitamin K-cholic acid mixture has been used throughout the work. In several instances a commercial preparation of vitamin K extracted from alfalfa (Klotogen, Abbott) has been used with satisfactory results.

*Results Obtained.*—In Chart I appear data showing a dramatic improvement in prothrombin concentration and cessation of bleeding on administration

\* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

of vitamin K-cholic acid mixture in obstructive jaundice. This patient had been operated upon a week previously and had not been given vitamin K. When first studied there was massive bleeding from the wound, and the prothrombin concentration was extraordinarily low, 9.8 per cent. Bleeding ceased and did not recur after vitamin K-cholic acid mixture was given the patient. Blood transfusion was given three days later to restore hemoglobin values. Plasma fibrinogen showed little change during the period of observation.

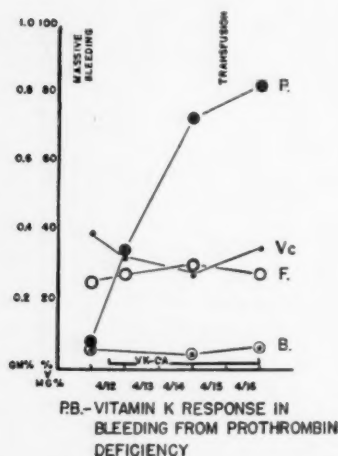


CHART 1.—Case P. B.: Vitamin K response in bleeding from prothrombin deficiency in obstructive jaundice. P. equals prothrombin concentration in per cent; Vc. equals cell volume in per cent; F. equals fibrinogen concentration in gm. per cent; B. equals plasma bilirubin concentration in mg. per cent. Vitamin K-cholic acid mixture 1.2 gm. per day given as shown.

Chart 2 shows prothrombin, fibrinogen and bilirubin values at various points in the management of a case of common duct obstruction from stone. The prothrombin level rose rapidly to a normal figure on giving vitamin K-cholic acid mixture before operation. The usual immediate postoperative drop took place, and the prothrombin concentration remained low until vitamin K-cholic acid mixture was given again, this time by jejunostomy. The sharp postoperative elevation of plasma fibrinogen is of interest, and shows the lack of correlation between prothrombin and fibrinogen changes.

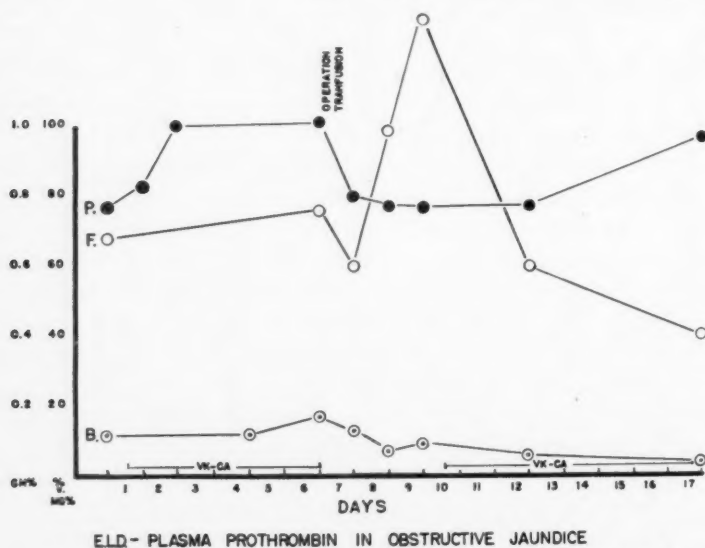


CHART 2.—Case E.L.D.: Plasma prothrombin in obstructive jaundice due to stone in the common duct. Vitamin K-cholic acid mixture 1.2 gm. per day given by jejunostomy after operation. P. equals prothrombin concentration in per cent; F. equals fibrinogen concentration in gm. per cent; B. equals plasma bilirubin concentration in mg. per cent.

# BLEEDING AND JAUNDICE

In Chart 3 are shown observations over a period of eight weeks in a case of stricture of the common duct. At the first operation the common duct was drained, but internal flow of bile was not established, and nearly complete external biliary fistula resulted. Since the patient was taking the regular hospital diet fairly well five days after operation it seemed justifiable to study the effect on prothrombin concentration of giving cholic acid without vitamin K.

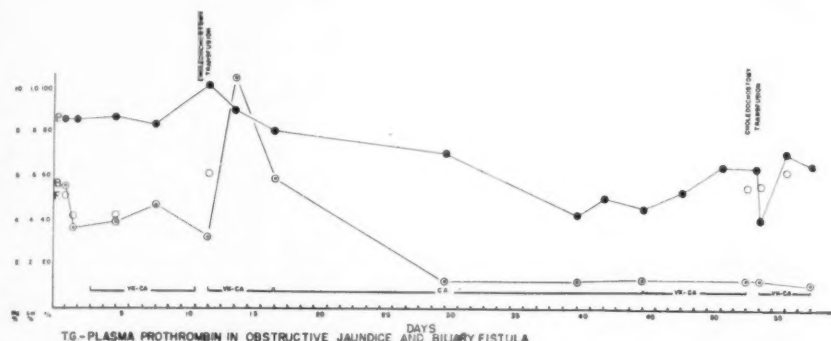


CHART 3.—Case T.G.: Plasma prothrombin in obstructive jaundice and biliary fistula. VK-CA. indicates administration of 1.2 gm. of vitamin K-cholic acid mixture per day; CA. indicates administration of 1.2 gm. of bile salts per day. P. equals plasma prothrombin in per cent; B. equals plasma bilirubin in mg. per cent; and F. equals fibrinogen in gm. per cent.

A gradual fall in prothrombin level resulted, and the low values persisted until vitamin K was again given the patient. Following the second operation the usual drop in prothrombin concentration with secondary response to vitamin K-cholic acid mixture is shown.

TABLE I

EFFECT OF OPERATION AND ANESTHESIA ON PLASMA PROTHROMBIN IN THE ABSENCE OF LIVER DISEASE. DETERMINATIONS IMMEDIATELY BEFORE AND AFTER OPERATION AND 24 HRS. LATER

	Vc %	Fibrinogen Gm./100 cc.	Plasma Protein Gm./100 cc.	Plasma Pro- thrombin %
P. R. Herniorrhaphy, spinal anes- thesia	49.2 47.3 54.1	0.26 0.25 0.41	7.02 6.95 8.06	95.0 94.0 91.0
L. S. Hysterectomy, ether anes- thesia	45.3 46.4 44.7	0.28 0.27 0.40	7.88 8.17 7.98	100.0 100.0 100.0
E. E. Hysterectomy, ether anes- thesia	40.7 41.1 40.5	0.27 0.26 0.40	7.54 7.50 7.23	90.0 95.0 98.0
I. S. Hysterectomy, ether anes- thesia	47.6 46.9 39.7	0.62 0.59 0.65	8.30 8.22 7.25	85.0 82.0 70.0
A. B. Abdominoperineal excision of rectum, spinal anesthesia	39.9 41.7 39.2	0.30 0.13 0.32	7.62 7.27 6.46	92.5 87.2 84.2

\* Denotes transfusion 500 cc. citrated blood.



Table I shows data obtained in a study of changes in concentration of prothrombin, plasma protein, fibrinogen and red cell hematocrit in five patients subjected to extensive operations under ether or spinal anesthesia. The absence of significant changes in prothrombin values in patients without liver disease is to be contrasted with the observations in Table II. In Table III are shown cell volume values, plasma fibrinogen and prothrombin concentra-

TABLE II

EFFECT OF OPERATION AND ANESTHESIA ON PLASMA PROTHROMBIN. E. L. D. AND L. C. FOR COMMON DUCT STONE; T. G. FOR EXTERNAL BILIARY FISTULA; E. W. FOR CARCINOMA OF PANCREAS. T. G. AND L. C. NOT JAUNDICED. DETERMINATIONS IMMEDIATELY BEFORE AND AFTER OPERATION AND 24 HRS. LATER

Operation	Vc %	Fibrinogen Gm./ 100 cc.	Plasma Protein Gm./ 100 cc.	Plasma Prothrom- bin %	Plasma Bilirubin mg. %
E. L. D. Cholecystostomy,	35.1*	0.76	6.51	101.1	17.8
choledochostomy	33.8	0.77	6.13	77.9	17.8
jejunostomy-novocain	40.0	0.60	6.60	80.0	13.3
E. W. Cholecystoduoden-	28.9*	0.79	6.31	91.9	8.6
ostomy, jejunostomy-	26.5	0.52	5.12	92.9	7.2
ether	33.8	0.60	6.13	77.6	6.6
T. G. Choledochostomy,	37.9*	0.57	8.57	52.2	
spinal-ether	40.0	0.53	8.32	65.8	
	41.3	0.58	7.63	41.6	
L. C. Cholecystectomy	44.2	0.20	8.15	110.0	
choledochostomy	45.1	0.27	7.76	97.6	
ether	42.8	0.46	8.30	87.8	

\* Denotes transfusion 500 cc. citrated blood.

TABLE III

EFFECT OF BLOOD TRANSFUSION ON PLASMA PROTHROMBIN. DETERMINATIONS BEFORE AND AFTER TRANSFUSION OF 600 CC. CITRATED BLOOD IN ADULT PATIENTS

Diagnosis	Vc %	Fibrinogen Gm./100 cc.	Prothrombin %
T. M. Chronic osteomyelitis	33.1	0.74	53.2
	31.8	0.57	60.5
O. S. Chronic lung abscess	35.9	0.53	61.1
	36.4	0.51	71.2
D. I. Obstructive jaundice	42.4	0.78	77.4
	43.7	0.75	88.4

tions, immediately before and after transfusion of 600 cc. citrated blood in adult patients. The increase in prothrombin values after transfusion in the three cases averages 9.5 per cent. In Tables IV and V are set down data illustrating the prothrombin response to vitamin K-cholic acid therapy before operation in obstructive jaundice due to stone and carcinoma. The maximal postoperative drop in prothrombin concentration in both groups of cases is tabulated with the time at which the drop occurred. The change in prothrom-

# BLEEDING AND JAUNDICE

TABLE IV

PLASMA PROTHROMBIN RESPONSE TO VITAMIN K-CHOLIC ACID THERAPY IN PATIENTS WITH OBSTRUCTIVE JAUNDICE DUE TO COMMON DUCT STONE. BLOOD TRANSFUSION PERFORMED AT OPERATION IN EACH INSTANCE. AVERAGE VALUES SHOWN BELOW. CHANGES EXPRESSED IN ABSOLUTE PERCENTAGE VALUES

		Prothrombin						
Age Sex	Duration Jaundice Weeks	Preoperative Response				Postop. Drop		
		Initial Value %	Change %	Duration Treatment Days	Vitamin K-Cholic Acid Gm.	%	Day	
L. H. S.	33-M.	8	49.8	+37.0	4	3.2	-8.9	3
T. G.	46-M.	Biliary fistula	43.6	+22.7	10	12.0	-24.7	1
D. F. W.	39-M.	2	35.7	+47.6	2	5.8	-45.6	3
M. L. K.	61-F.	8	70.7	+29.3	5	6.0	-57.9	9
E. L. D.	70-F.	2	77.8	+23.3	6	*	-24.2	2
R. D.	35-M.	1	47.1	+43.2	2	1.8	-23.2	3
J. M. S.	63-M.	1.5	72.9	+19.7	5	6.0	-3.8	2
G. K.	71-F.	4	81.3	+27.5	3	3.6	-15.3	1
J. M. S.	34-F.	0.5	95.0	+15.0	6	3.6	-39.1	4
R. M.	69-F.	8	53.4	+51.7	4	**	-20.4	1
D. P.	22-F.	1.5	68.6	+31.4	3	3.6	-15.7	2
Av.		3.6	64.9	+31.7	4.5	5.1	-25.3	2.8

\*Received daily 6,000 units vitamin K (Almquist-Stokstad) with bile salts.

\*\*Received daily 3,000 units with bile salts.

TABLE V

PLASMA PROTHROMBIN RESPONSE TO VITAMIN K-CHOLIC ACID THERAPY IN PATIENTS WITH OBSTRUCTIVE JAUNDICE DUE TO CARCINOMA. BLOOD TRANSFUSION PERFORMED AT OPERATION IN EACH INSTANCE. AVERAGE VALUES SHOWN BELOW. CHANGES EXPRESSED IN ABSOLUTE PERCENTAGE VALUES

		Prothrombin						
Age Sex	Duration Jaundice Weeks	Preoperative Response				Postop. Drop		
		Initial Value %	Change %	Dura- tion Treat- ment Days	Vitamin K-Cholic Acid Gm.	%	Day	
J. B.	47-M.	3	71.4	+15.2	5	4.0	-17.7	2
H. C. K.	32-F.	4	71.1	+24.6	4	3.2	-25.0	4
P. W.	58-M.	5	28.9	+67.2	3	9.0	-30.4	7
J. R. B.	53-M.	4	83.2	+16.8	6	24.8	-10.0	4
T. P. H.	66-M.	6	28.0	+28.7	2	5.7	-18.6	4
E. W.	73-F.	8	23.1	+68.8	9	10.8	-14.3	1
D. N. I.	42-M.	12	69.9	+9.3	4	5.2	-10.0	1
W. T. M.	54-M.	4	67.6	+13.8	9	11.2	-29.5	4
Av.		5.8	55.4	+30.5	5.2	9.2	-19.4	3.4

bin is expressed in absolute percentage and not percentage of the previous value. The amount of vitamin K-cholic acid mixture taken in each instance is recorded. The postoperative drop in plasma prothrombin occurred invariably in both groups of cases. In interpreting this finding allowance must be made for the fact that every patient had a blood transfusion at the end of the operation, which effects an immediate increase of from 6 to 10 per cent in prothrombin concentration.

*Discussion.*—It is clear that plasma prothrombin concentration in obstructive jaundice is a labile quantity. The value rises rapidly under treatment with vitamin K-cholic acid mixture, and falls quickly under such depressing circumstances as infection, surgical operation, hemorrhage and anesthesia. This implies a lack of reserve prothrombin in obstructive jaundice and suggests the need for studying prothrombin concentration closely in managing these cases. In the more depleted patients we have performed jejunostomy at the time of operation on the biliary tract to avoid delay in the further administration of vitamin K-cholic acid mixture, as well as for feeding. This may occasionally be necessary in preparing a patient for operation on the biliary tract, particularly if veins are poor and the patient not thoroughly cooperative.

In connection with the immediate drop in prothrombin concentration after operation, an interesting question is the effect of the anesthetic agent. Evidence at hand suggests that the same depression of prothrombin level is seen after ether, spinal, or local novocain anesthesia, but the question needs further study. As seen in Table I, major surgical procedures in patients without liver disease may be performed under spinal or ether anesthesia without changes in prothrombin concentration. It is probable the patient with obstructive jaundice has depleted prothrombin reserves compared with the normal, and that the liver in obstructive jaundice is less resistant to depressing conditions.

In comparing the cases of obstructive jaundice due to stone with those due to carcinoma, it is apparent that the initial average prothrombin concentration is higher in the former group, the response to vitamin K-cholic acid therapy is more rapid, the dosage is smaller and the final preoperative prothrombin concentration is nearer normal. Hard and fast conclusions are hardly justifiable without further observations, but the data at hand suggest that the patients with carcinomatous obstruction have greater liver damage and are more likely to show pathologic bleeding. The danger from pathologic bleeding comes with prothrombin concentrations below 40 per cent, and the average preoperative and postoperative concentrations in these cases were well above this figure.

In considering the dosage of vitamin K-cholic acid mixture necessary to restore prothrombin concentration to a safe level, the extent of liver damage is of much importance. The data shown in Chart 3 are of interest in this connection. This patient had common duct stricture with a high degree of liver damage from biliary cirrhosis. After the first operation, which resulted in external biliary fistula, the patient was given cholic acid without vitamin K.

Despite the fact that the standard hospital diet was being taken fairly well the prothrombin concentration fell gradually, and the low values persisted until vitamin K was again given the patient. We have had the experience in other patients of failing to get a satisfactory response in plasma prothrombin until the dose of vitamin K-cholic acid preparation usually sufficient was doubled, although in no case has failure to respond been complete. These have been patients with clinical signs of severe liver damage. These findings suggest the applicability of the law of mass action in this connection and indicate that the quantity of vitamin K given must be increased in the presence of factors hindering prothrombin formation.<sup>7</sup>

In treating prothrombin deficiency in obstructive jaundice the importance of measures which restore liver function, minimize liver damage, and favor renal function should be pointed out. A daily carbohydrate intake of 400 to 600 Gm., proper fluid therapy, and early decompression of the obstructed biliary tract are very helpful measures. In the desperately sick patient with complete biliary obstruction from carcinoma a two-stage operative plan is often desirable, the first operation being drainage of the distended gallbladder under novocain anesthesia after two to four days of preparation. Patients with obstructive jaundice have usually lost much weight and are in a state of general malnutrition. Cevitamic acid, vitamin B complex, and vitamins A and D should be given by mouth, or suitable preparations may be given parenterally. Finally, blood transfusion is often necessary as the most rapidly effective measure in dealing with reduction in hemoglobin and plasma protein. It has been our routine practice to give the patient a blood transfusion at the time of operation on the biliary tract.

#### CONCLUSIONS

(1) Plasma prothrombin concentration is reduced in obstructive jaundice, and may undergo a further drop immediately after operation.

(2) Prothrombin deficiency has invariably responded to proper vitamin K-cholic acid therapy, but larger doses and longer treatment were required in more severe grades of liver damage.

(3) The therapeutic importance of adequate intake of carbohydrate, proper fluids and other vitamins and of blood transfusion should be emphasized.

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DISCUSSION.—DR. ARTHUR W. ALLEN (Boston): Any large general hospital might consider themselves fortunate to have a surgeon competent to make a study such as Doctor Stewart has just presented, not only sufficient chemical knowledge to follow these patients but also to make his own vitamin K. It may not require a great deal of skill to boil down a hundred bushels of spinach in order to make this extract, but it is time-consuming.

Also, the prothrombin level determinations that must be made on these patients, in order to follow them accurately, is a very heavy burden on his laboratory, and this brings up a point which I wish to stress. As these new laboratory principles are evolved from the research department, and found essential in the routine care of patients, they must be taken over by the general laboratory and this creates an extra burden. I had hoped that Doctor Stewart might be able to find a simple method of determining how much vitamin K and cholic acid might be required in a jaundiced patient and how many days of treatment were necessary without having to follow so closely the prothrombin levels. Unfortunately, we have not been able, up to date, to formulate these requirements on a satisfactory basis other than by accurate laboratory data.

The other point that I wish to bring up is a technical one. I am quite sure in these very ill patients that it is wise to add a jejunostomy in order to be sure that you can continue to administer vitamin K and cholic acid immediately after operation. Many of these patients will not be able to take the mixture by mouth for a few days and will have a very definite drop in prothrombin level. Thus we may avoid a dangerous hemorrhagic stage and not be faced with emergency measures.



THE SIGNIFICANCE OF THE CHOLESTEROL PARTITION  
OF THE BLOOD SERUM IN SURGERY OF THE  
GALLBLADDER\*

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THE ADVENT of more accurate procedures for the estimation of cholesterol and its fractions in the blood serum has resulted in renewed interest in the rôle played by the liver in cholesterol metabolism. Any assumption that one can translate abnormal cholesterol findings into terms of liver function should be dismissed, since any one test has as yet failed to measure the many diverse functions of the liver. It is not within the scope of this paper to discuss the ever increasing accumulation of experimental data on the relationship between cholesterol metabolism and the liver, nor will any attempt be made to review the large amount of literature on liver function in general. There are, however, certain definite facts regarding the metabolism of cholesterol and its fractions, and their relationship to the liver which form the basis of our investigations and their clinical significance as reported in this paper. These are:

(1) The concentration of the total cholesterol in the blood serum of each normal individual in health, is maintained at a constitutional level, which is characteristic for that individual, and is not subject to large deviations.<sup>1,2,3</sup>

(2) There is a definite relationship between the amount of free and total cholesterol in normal persons. The percentage of free in total cholesterol appears to be a physiologic constant. The amount of free cholesterol in healthy adults varies between 24.3 and 30 per cent, with an average of 26.9 per cent of the total cholesterol.<sup>4,5</sup>

(3) Changes in the ratio of free to total cholesterol are of considerably greater significance than changes in the concentration of total cholesterol; although, even in normal individuals there are wide variations, the concentration for the same individual, in health, is constant.

It is generally believed that esterification of cholesterol esters from cholesterol and the higher fatty acids is accomplished by the liver.<sup>6,7</sup> The liver also has the ability through cholesterol esterases to hydrolyze cholesterol esters. The maintenance of this reversible reaction is a normal physiologic process of the liver, which, we believe, can be measured by the determination of the cholesterol partition of the blood serum.

As stated above, in normal individuals the ratio of esterified to free cholesterol is a physiologic constant. Any alteration in this relationship, *i.e.*, a rise

\* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

in the percentage of free cholesterol, with a corresponding decrease in ester cholesterol, regardless of the amount of total cholesterol, indicates a disturbance in the ability of the liver to regulate the synthesis and hydrolysis of cholesterol esters, a disturbance which has been explained by Thannhauser and Schaber<sup>8</sup> on the basis of damage to the hepatic cells.

We believe that the liver has a functional reserve, which is reflected by changes in the cholesterol partition. A rise in the percentage of free cholesterol of the blood serum is indicative of a lowering of the functional reserve. This would be analogous to the CO<sub>2</sub> combining power of the blood plasma as a measure of the alkaline reserve in acidosis. Therefore, throughout this paper we will refer to changes in the per cent of free cholesterol as a measure of the functional reserve of the liver. We propose to show that the demonstration of changes in the cholesterol partition is of clinical value in determining the functional reserve of the liver in hepatic disturbances, associated with surgery of the biliary tract, and, as such, serves to indicate the optimum time for a planned surgical intervention.

*Procedures.*—The technical methods employed for the determination of total cholesterol were those described by Bernhard and Dreker,<sup>9</sup> Dreker, Bernhard and Leopold,<sup>10</sup> and Bernhard.<sup>11</sup> Free cholesterol was determined by the modification of the Schoenheimer and Sperry technic described by Dreker, Sobel and Natelson.<sup>12</sup> Ester cholesterol determinations were made on the supernatant fluid and washings, after precipitation of the free cholesterol, by evaporation to dryness, extraction with petroleum ether, again evaporated and dried, and the residue taken up with chloroform and the cholesterol determined as in total cholesterol. The icterus index was determined by the method described by Bernhard and Maue, cited by Stetten.<sup>13</sup> In all our investigations the blood was obtained before breakfast, the serum separated and the determinations made as soon as possible. Serum was used, because Sperry and Schoenheimer<sup>14</sup> have shown that oxalated plasma contains significantly smaller amounts of total and free cholesterol than either serum or heparinized plasma from the same sample of blood.

*Normal Values.*—With our technical methods, our own normal figures in 51 healthy adults were as follows: Total cholesterol varied between 141 and 404 mg. per 100 cc. of serum. Free cholesterol varied between 31 and 110 mg. per 100 cc. of serum. The per cent of free cholesterol varied between 16 and 30, with an average of 23 per cent. These figures compare with those reported by Sperry.<sup>4</sup>

*Clinical Material.*—We have classified our cases into three groups:

(A) Cases of acute and chronic cholecystitis and cholelithiasis in which operation was performed and in which the cholesterol partition was within normal limits.

(B) Patients operated upon showing a high percentage of free cholesterol.

(C) Nonoperated cases showing an increased percentage of free cholesterol.

Group A.—Cases of acute and chronic cholecystitis and cholelithiasis in

# THE CHOLESTEROL PARTITION

which operation was performed and in which the cholesterol partition was within normal limits indicating a normal functional reserve of the liver (Table I).

This group also included four patients who showed an initial decreased functional reserve as revealed by the increase in the percentage of free cholesterol. These four patients received the usual medical treatment including a low fat, high carbohydrate diet, with additional forced glucose ingestion. Under this regimen there was an improvement in the functional reserve as shown by a drop to normal values in the percentage of free cholesterol. In

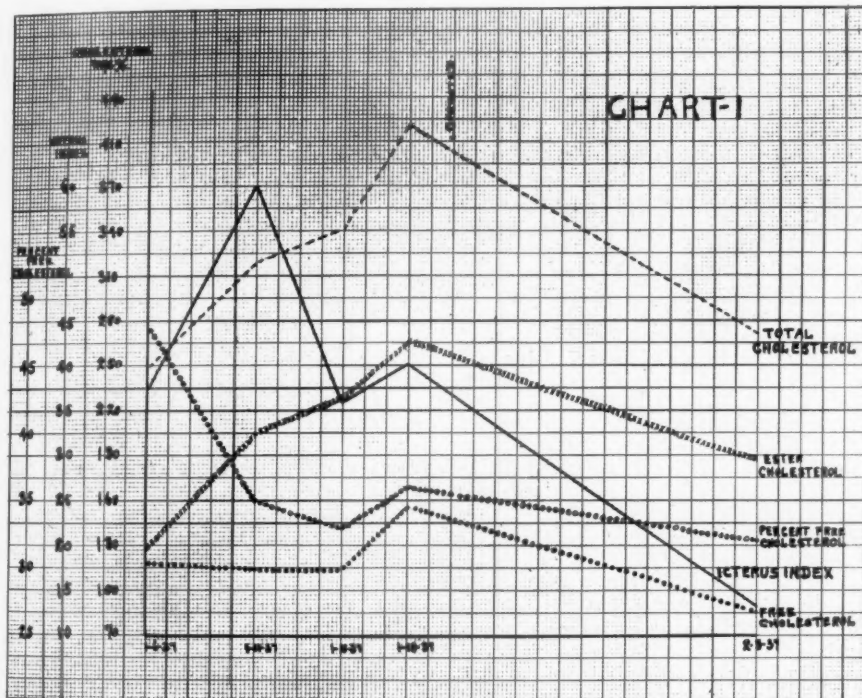


CHART I.—Case 1: Hosp. No. 55835: Chronic cholecystitis and cholelithiasis with initial diminished functional reserve, which returned to normal preoperatively after medical treatment. Good postoperative course.

these patients operation was delayed until the functional reserve was restored. A typical case (Case 1: No. 55835) is graphically illustrated in Chart I.

**Case 1.**—Hosp. No. 55835: A white female, age 46, complained of sharp pain in the right upper quadrant, and jaundice of ten days' duration, with clay-colored stools and dark urine. There were two previous attacks, similar in nature, 5 and 11 months before the present attack. Her temperature, pulse and respiration were normal. Examination of the abdomen revealed tenderness in the right upper quadrant and a palpable mass two fingers' breadth below the right costal border. The pertinent laboratory findings were: Wassermann negative, icterus index 37, total cholesterol was 246, ester 128, and the free cholesterol 118 mg. (48 per cent). A diagnosis of chronic cholecystitis and cholelithiasis was made. The patient was placed upon the routine medical treatment because the cholesterol partition revealed a low functional reserve of the liver. The cholesterol

TABLE I  
CASES OPERATED UPON IN WHICH THE CHOLESTEROL PARTITION WAS WITHIN NORMAL LIMITS

Hist. No.	Age	Sex	Date	Icterus Index	Serum Cholesterol Mgs. Per 100 Cc.		Per Cent Free Choles- terol	Diagnosis and Remarks
					Total	Ester		
49058	50	F.	6-19-36	42	220	140	80	Acute cholecystitis and cholelithiasis. Operation: 6-23-36—Cholecystectomy.
55452	34	F.	12-8-36	47	240	160	80	Chronic cholecystitis and cholelithiasis.
704	45	F.	12-12-36	14	181	125	56	Operation: 12-14-36—Cholecystectomy
			12-28-36	8.3	226	166	60	
			2-5-37	21.4	254	174	80	Chronic cholecystitis and cholelithiasis.
39365	45	M.	2-18-37	11	245	161	84	Operation: 2-8-37—Cholecystectomy Chronic cholecystitis and cholelithiasis.
27811	57	F.	6-16-37	57	232	160	72	Operation: 2-19-37—Cholecystectomy. 3-1-37—Pulmonary embolus—Death
37820	66	F.	6-25-37	22	205	135	75	Chronic cholecystitis and cholelithiasis.
			10-9-37	60	275	195	80	Operation: 7-12-37—Cholecystectomy. Stones in common duct
60450	32	F.	10-18-37	19	268	188	80	Acute cholecystitis and stone in common duct.
61273	59	M.	10-20-37	25	232	172	60	Operation: 10-25-37—Cholecystectomy and choledochotomy
			10-27-37	10	212	156	56	Chronic cholecystitis and cholelithiasis.
			12-15-37	50	209	145	64	Operation: 10-28-37—Cholecystectomy
			12-20-37	20	288	223	66	Chronic cholecystitis and cholelithiasis. Operation: 1-11-38—Cholecystectomy

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Chronic cholecystitis and cholelithiasis.  
Operation: 1-11-38—Cholecystectomy

66264	59	F.	2-17-38	6.6	280	200	80	28	Chronic cholecystitis and cholelithiasis. Operation: 2-21-38—Cholecystectomy
54347	47	M.	2-18-38	7.5	256	196	60	23	Chronic cholecystitis and cholelithiasis. Operation: 2-21-38—Cholecystectomy
61251	36	M.	1-21-38	25	185	133	52	28	Fistula of common duct. Operation: 3-16-38—Revision and implantation of common duct into duodenum.
			2-7-38	40	206	152	54	26	Previous operation: 12-18-37—Cholecystectomy
			2-14-38	33	150	106	44	29	
			2-24-38	62.5	183	123	60	32	
			2-28-38	44	146	98	48	33	
52439	44	M.	5-23-36	120	212	102	100	47	Acute cholecystitis and cholelithiasis. Operation: 5-29-36—Cholecystectomy. Preoperative treat- ment
			5-27-36	33	216	146	72	33	
55835	46	F.	1-6-37	37	246	128	118	48	Chronic cholecystitis and cholelithiasis. Stone in common duct.
			1-11-37	60	319	205	114	35	
			1-15-37	36	342	228	114	33	Operation: 1-20-37—Cholecystectomy and drainage of com- mon duct.
			1-18-37	40	421	266	155	36	Preoperative treatment
			2-3-37	13.3	271	184	87	32	Chronic cholecystitis and stones in cystic and common ducts. Operation: 11-9-38—Cholecystectomy.
66159	59	F.	10-29-38	51	355	195	160	45	Preoperative treatment
			11-2-38	72	353	213	140	39	Chronic cholecystitis and cholelithiasis. Stone in common duct.
			11-22-38	22	297	228	69	23	Operation: 11-30-38—Cholecystectomy. Drainage of com- mon duct.
66220	48	F.	11-1-38	93	346	118	228	66	Preoperative treatment
			11-12-38	70	548	320	228	42	
			11-16-38	60	394	266	266	32	



examinations were repeated five days later, and showed a decrease in the percentage of free cholesterol to 35 per cent although there was a rise of the icterus index to 60. The same treatment was continued and four days later there was a decrease in the free cholesterol to 33 per cent and a marked drop in the icterus index to 36. Examinations made three days later showed about the same values for the cholesterol partition, and it was thought that this was the opportune time to operate since improvement in the functional reserve was so evident.

At operation a gallbladder filled with stones was found, as well as a stone in the common duct. Cholecystectomy and removal of the common duct stone were done. The patient made an uneventful recovery. Two weeks after operation the cholesterol partition was determined, and the free cholesterol was 32 per cent.

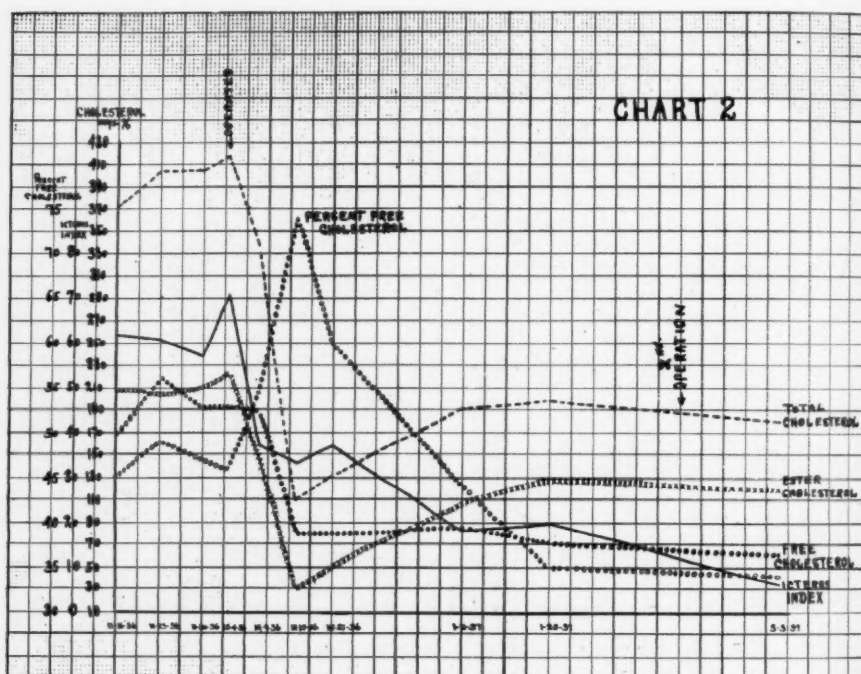


CHART 2.—Case 2: Hosp. No. 55111: Chronic cholecystitis with decreased functional reserve—not improved by medical treatment. The percentage of free cholesterol was increased at time of operation. Stormy postoperative course.

COMMENT.—This case and the other three similar cases in this group showed at the time of admission that there was a lowered functional reserve of the liver as demonstrated by the increase of the percentage of free cholesterol in the serum. After preoperative therapy, improvement in the reserve was reflected by decrease in the free cholesterol per cent, and when this value returned to normal it was believed that the patient was in better condition to withstand surgical intervention.

All the other patients comprising this group in which the percentage of free cholesterol was normal, indicating good functional reserve of the liver, had a smooth postoperative course.

Group B.—Patients operated upon showing a high percentage of free cholesterol (Table II).

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CASES OPERATED UPON WHICH SHOWED A HIGH PERCENTAGE OF FREE CHOLESTEROL AT TIME OF OPERATION

TABLE II

Hist. No.	Age	Sex	Date	Icterus Index	Serum Cholesterol Mg. Per 100 Cc.			Per Cent Free Choles- terol	Diagnosis and Remarks
					Total	Ester	Free		
55111	43	F.	11-16-36	62	373	208	168	45	Chronic cholecystitis. Operation: 12-4-36—Cholecystectomy and drainage of com- mon duct. No stones found, but common duct markedly dilated. Operation: 2-15-37—Cholechohorraphy.
			11-23-36	61	404	204	200	49	
			11-30-36	57	405	213	192	47	
			12-4-36	71	417	225	192	46	
			12-9-36	37	337	149	188	55	
			12-15-36	33	108	28	80	74	
			12-21-36	37	132	52	80	60	
			1-11-37	18	191	107	84	44	
			1-25-37	20	198	128	70	35	
			3-3-37	6	180	118	62	34	
56175	62	F.	1-27-37	125	286	113	173	60	Carcinoma of gallbladder with metastases to liver. Operation: 2-1-37—Celiotomy
			2-9-37	143	230	70	160	70	
			2-18-37	140	228	42	186	81	
			6-10-37	62.5	218	118	100	45	
			6-16-37	53	222	136	86	39	
58381	50	F.	6-22-37	71	163	87	76	46	Chronic cholecystitis and cholelithiasis. Operation: 6-18-37—Cholecystectomy and drainage of com- mon duct. 7-4-37—Expired. Necropsy—Hepatitis. Syphilis of the liver. Complete obstruction of common duct. Operation: 2-28-36: Liver drainage. Operation: 11-28-36: Hepatoduodenostomy. 1-9-37—Expired
			6-12-36	174	132	70	62	46	
			10-9-36	44	439	276	163	37	
			10-31-36	89	494	204	290	58	
			11-10-36	222	258	70	188	73	
P11152	42	M.	11-18-36	133	360	160	200	55	
			12-10-36	47	214	100	114	53	
			12-26-36	31	186	110	76	40	

This group consists of four cases in which the percentage of free cholesterol was definitely increased. The course of Case 2, Hosp. No. 55111, typical of this group, is shown graphically in Chart II.

**Case 2.**—Hosp. No. 55111: A white female, age 43, was admitted, November 14, 1936, complaining of increasing jaundice and intermittent epigastric pain, radiating to the back, of four weeks' duration. The stools were clay-colored, urine very dark brown. There was occasional nausea but no vomiting. Patient had been treated for syphilis 17 years before, and at that time had also been jaundiced. Temperature, pulse and respiration were normal. Examination of the abdomen revealed generalized tenderness, most marked in the epigastrium and right upper quadrant. The icterus index was 62, total cholesterol 373, ester 208, free cholesterol 168 (45 per cent). Feces showed presence of bile. The Wassermann and Kline tests were both negative. A special Graham series, the dye being administered over a period of four days, showed no definite pathology. Due to the fact that the initial percentage of free cholesterol was increased, showing a lowered functional reserve of the liver, it was decided to place the patient under routine medical treatment. During the next two weeks, the percentage of free cholesterol increased slightly, being 49 and 47 per cent, and the icterus index 61 and 57 respectively. The patient during this period showed neither clinical nor functional reserve improvement. On December 3, 1936, 20 days after admission, patient had severe attacks of right upper quadrant pain, and it was thought she might have a stone in the common duct. Operation was advised. Icterus index rose to 71 on the following day, and the percentage of free cholesterol remained approximately the same (46 per cent) still indicating poor functional reserve.

At operation December 14, 1936, a chronically inflamed gallbladder was found, and the common bile duct was dilated, but no stones were found. Cholecystectomy and drainage of the common duct were performed. Nothing abnormal was felt in the pancreas. The postoperative course was extremely stormy from the very onset, with a rise of temperature to 104° and 105° F., pulse 120, and respiration 22 for the first three days. Intravenous therapy of saline and glucose was given almost continuously. Five days postoperative, the icterus index fell to 37, but there was a definite rise in the percentage of free cholesterol to 55 per cent. The spiking temperature continued, and then several hemorrhages from the wound occurred which were controlled after transfusions. Ten days postoperative, there was a sharp drop in the total cholesterol to 108 mg., with a marked rise in the free cholesterol percentage to 74 per cent. Icterus index was 33. The course continued to be stormy, and one week later the total cholesterol began to rise while the percentage of free cholesterol had decreased to 60 per cent. The patient began to improve gradually. About one month after operation, the stools again became clay-colored and there was profuse bile drainage from the wound (the T-tube had been removed on the seventeenth postoperative day). The icterus index on January 11 was 18, and the percentage of free cholesterol was 44, showing a definite improvement in the functional reserve of the liver. Two weeks later there was continued clinical improvement, and on January 25 the free cholesterol was 35 per cent, indicating further recovery in the functional reserve. Because of the biliary fistula, a second operation was considered and it was thought that due to the improved functional reserve, surgical intervention would be well tolerated at this time.

Accordingly, a secondary reconstruction of the common bile duct was performed, February 15, 1937. The postoperative course was entirely different from that following the original operation. There was only a slight rise in temperature which quickly returned to normal, and the patient made an otherwise uneventful recovery. A follow-up of this patient, March 3, 1937, showed that the icterus index was normal, being 6, and the percentage of free cholesterol was 34. On December 9, 1937, an exploratory operation was performed upon this patient at another hospital, because of recurring symptoms. A primary carcinoma of the pancreas with metastases to the liver was found, and the patient expired December 21, 1937.

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**COMMENT.**—In this patient, the initial determination of the cholesterol partition of the blood serum revealed a high value for the percentage of free cholesterol, indicating a decreased functional reserve of the liver. It will be observed that up to the time of the first operation there was a slow but definite rise in the percentage of free cholesterol. It will also be noticed that after operation the patient developed fever with a marked drop in the concentration of total cholesterol. In spite of this continued increase in temperature, the total cholesterol began to rise and the free cholesterol percentage had started to fall which is quite in keeping with McQuarrie's and Stoesser's<sup>15</sup> observation that there is no constant relationship between the height of fever and degree of hypocholesterolemia. As the free cholesterol percentage continued to fall, indicating improvement in the functional reserve, there was also a marked clinical improvement in the condition of the patient. There was almost a normal percentage at the time of the second operation. The fact that the patient's second postoperative course was uneventful, we assumed to be on the basis of a marked improvement in the functional reserve. This case illustrates the value of frequent determinations of the cholesterol partition as a guide in prognosis.

**Case 3.**—Hosp. No. P56175: A white female, age 62, was admitted, January 26, 1937, complaining of epigastric distress and painless jaundice of one month's duration. The stools were light yellow in color, and the urine was dark. Examination of the abdomen revealed slight tenderness in the right upper quadrant, and the liver was palpable two fingers' breadth below the right costal border. Temperature, pulse and respiration were normal. Important laboratory findings were: Icterus index 125, total cholesterol 286 mg., ester 113 and the free cholesterol 123 mg. (60 per cent), indicating a lowered functional reserve. A plain film of the abdomen revealed a shadow which was interpreted as a stone in the fundus of the gallbladder. Preoperative medical treatment was not instituted.

At operation, January 31, 1937, five days after admission, an inoperable carcinoma of the gallbladder with metastases to the liver and pancreas was found. The postoperative course was poor, the icterus index rising to 143 and the free cholesterol to 70 per cent. One week later, the icterus index was 140 with a further rise in the percentage of free cholesterol to 81 per cent. The patient's clinical condition became gradually worse, and she expired six weeks later.

**COMMENT.**—From the very onset, the examination of the serum of this patient revealed a marked increase in the percentage of free cholesterol showing diminished functional reserve which, postoperatively, became progressively worse.

**Case 4.**—Hosp. No. 58381: A white female, age 50, was admitted, June 10, 1937, complaining of three attacks of upper abdominal pain radiating to the back. The first attack occurred one and a half years before admission. The present attack was accompanied by nausea, vomiting and jaundice of four days' duration. Temperature, pulse and respiration were normal. There was moderate tenderness in the right upper quadrant of the abdomen, and a small rounded mass was thought to be felt just below the right costal margin. Laboratory examinations revealed a negative Wassermann, icterus index was 62.5, total cholesterol was 218 mg., ester 181 mg. and free cholesterol 100 mg. (45 per cent), showing a diminished functional reserve. A roentgenogram of the abdomen revealed several calcified shadows which were thought to be faceted gallstones. The patient

was placed on medical regimen for a week, at which time the icterus index was 53 and the percentage of free cholesterol was 39.

At operation, June 18, 1937, a small contracted gallbladder containing a stone, and two stones in the common duct were found. Cholecystectomy and drainage of the common duct was performed. Postoperatively, this patient did not do well. The jaundice increased and the temperature was elevated. Four days postoperative, there was marked nausea and vomiting and the icterus index was 71, the percentage of free cholesterol being 46. The patient was given almost continuous intravenous infusions of saline and glucose. During the following days, there was a sanguineous discharge from the wound. Transfusion was given. She continued to bleed intermittently for the next few days and her condition became very poor. She expired two weeks after operation. Postmortem examination was performed and a diffuse hepatitis with necrosis of the liver cells was found.

COMMENT.—This patient also showed a poor preoperative functional reserve without postoperative improvement, associated with a stormy postoperative course and death.

**Case 5.**—Hosp. No. P11152: A white male, age 42, was admitted, February 20, 1936, with a history of increasing jaundice and general abdominal pains, chills and fever for the past six weeks. There was a past history of intestinal amebic infection and treated syphilis. Laboratory findings showed an absence of bile in the stool, an icterus index of 100, Wassermann 4+ and Kline 4+. Examination of the abdomen revealed a greatly enlarged liver with its edge extending eight centimeters below the costal margin. The edge was sharp and not tender. The spleen was moderately enlarged. There were no paraumbilical dilatations of the superficial veins. Roentgenologic examination showed no evidence of stones but a markedly enlarged liver.

An exploratory operation, February 28, 1936, revealed an enlarged, congested liver, a thickened gallbladder containing no bile or stones, a completely fibrosed and nonpatent common duct, and an exceedingly hard, constricting mass at the junction of the right and left hepatic ducts in the liver. This contained mucopurulent material which, on immediate examination, showed no ameba. The head of the pancreas was enlarged and hard. A piece of the liver was excised for further examination and because no drainage could be instituted into the common duct, two large tubes were inserted into the liver itself in the region of the hepatic ducts.

The patient had a very stormy postoperative convalescence but began to improve after the fifth day when bile appeared through the drainage tube. The pathologic report was syphilitic granuloma of the peritoneum, small gumma of the liver with acute and chronic hepatitis and bile stasis. The patient gradually improved with occasional remissions, care being taken to keep the drainage tubes open and bile escaping to the surface. His jaundice disappeared, but at no time was there any bile in the stool. Fresh pig's bile was fed him daily. He left the hospital 14 weeks later for further convalescence at which time the cholesterol partition showed a free cholesterol of 46 per cent.

He returned to the hospital, October 6, 1936, with a history of lessening bile drainage, increasing jaundice, fever and chills, loss of weight and general malaise. Antisyphilitic treatment was continued. In view of the general course of the disease, it was decided to attempt an anastomosis between the liver and the duodenum. At this time, as shown in Table II, the percentage of free cholesterol was 37. On October 31, the icterus index was 89 and the free cholesterol 58 per cent, showing further decrease in functional reserve, and in addition the permanent biliary fistula was markedly contracted. On November 10, there was a decided increase both in the percentage of free cholesterol and icterus index. The former was 73 and the latter 222.

The second operation was performed November 28, 1936, and the same pathologic conditions as previously observed were again found. An anastomosis between the right lobe of the liver and the duodenum was performed, and two large drainage tubes also placed directly into the liver. Pathologic examination of the removed tissue was reported



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as chronic hepatitis (biliary cirrhosis); no evidence of malignancy. The patient again had a very stormy convalescence followed by a period of improvement as soon as bile drainage became established. The anastomosis held for several weeks with the appearance of bile in the stool, and then a duodenal fistula appeared. During the next three weeks, the percentage of free cholesterol remained elevated, but there was a drop in the icterus index. These values remained practically unchanged, until fatal termination of the disease, January 9, 1937.

COMMENT.—This case was apparently one of syphilis of the liver with increasing fibrosis causing complete biliary obstruction. There was evidence

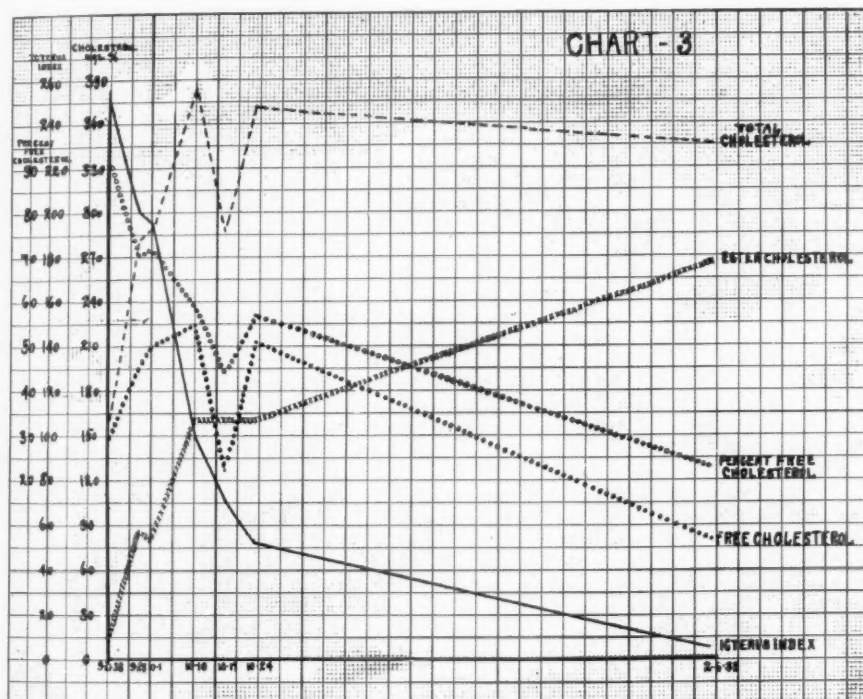


CHART 3.—Case 6: Hosp. No. 65549: Catarrhal jaundice. Nonoperated case. Very high percentage of free cholesterol on admission which gradually returned to normal under medical treatment. Case illustrates the prognostic value of the cholesterol partition.

of poor functional reserve with no improvement during the postoperative course, indicating a poor prognosis.

Group C.—Nonoperated cases showing an increased percentage of free cholesterol (Table III).

This group consists of eight cases of catarrhal jaundice studied over a period of time, three cases of portal cirrhosis, one case of cholecystitis and cholelithiasis, and one case of gangrenous cholecystitis. Detailed observations of Case 6, Hosp. No. 65549 are shown graphically in Chart III, and this case will be discussed in order to show the value of the cholesterol partition in a patient with a questionable surgical diagnosis.

Case 6.—Hosp. No. 65549: A white male, age 57, was admitted, September 20, 1938, complaining of painless jaundice of four weeks' duration. There was anorexia and loss

TABLE III  
CASES NOT OPERATED UPON WHICH SHOWED AN INCREASED PERCENTAGE OF FREE CHOLESTEROL

Hist. No.	Age	Sex	Date	Icterus Index	Serum Cholesterol Mg. Per 100 Cc.			Per Cent Free Choles- terol	Diagnosis and Remarks
					Total	Ester	Free		
52139	34	M.	5-7-36	227	213	109	104	49	Catarrhal jaundice
			5-11-36	133	211	108	103	48	
			5-15-36	71.5	216	128	86	40	
			5-26-36	29	205	131	74	36	
			6-2-36	22	257	177	80	30	
52802	33	M.	6-26-36	10	169	112	57	33	Catarrhal jaundice
			6-9-36	143	205	95	110	54	
			6-16-36	142	164	50	114	69	
			6-22-36	142	222	106	116	57	
			6-30-36	142	230	106	124	54	
54588	47	M.	10-10-36	172	225	62	163	72	Catarrhal jaundice
			10-16-36	165	178	30	148	80	
			10-24-36	100	173	39	134	77	
			10-29-36	77	274	128	146	56	
			11-10-36	37.5	214	114	100	46	
54691	38	F.	11-17-36	28	208	130	78	37	Catarrhal jaundice
			11-23-36	20	185	116	69	37	
			10-16-36	104	242	94	148	61	
			10-22-36	80	254	80	174	68	
			10-28-36	35	204	122	82	40	
54753	65	F.	11-4-36	31	192	116	76	40	Acute cholecystitis and cholelithiasis. 10-24-36—Patient passed gallstone
			10-21-36	49	197	111	86	43	
			10-26-36	23	253	119	134	53	
			10-31-36	20	194	122	72	37	
			11-11-36	14	152	114	38	25	

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54947	42	F.	11-17-36	24	160	71	89	55	Portal cirrhosis.
			12-4-36	30	180	100	100	55	
			12-17-36	25	190	106	84	44	
			10-14-37	22	215	127	88	41	
P12538	37	F.	2-24-37	66	168	58	110	65	Necropsy: 3-16-38
			3-5-37	50	335	139	196	58	Catarrhal jaundice
			3-12-37	25	247	163	84	34	
58730	46	F.	6-30-37	66.5	200	113	87	43	Catarrhal jaundice
			7-2-37	100	220	98	122	55	
			7-8-37	80	246	80	166	67	
			7-15-37	33	245	148	97	39	
			7-22-37	28	195	153	42	21	
			11-16-37	8	211	175	36	17	
55612	7	F.	10-19-37	25	540	280	260	48	Gangrenous cholecystitis with rupture of gallbladder.
			10-22-37	62.5	466	296	190	40	Cholelithiasis. Acute generalized peritonitis. Liver abscesses.
			10-26-37	62	436	246	190	43	Necropsy: 2-9-38
			11-8-37	83	183	69	114	62	
			11-16-37	36	148	72	76	51	
			11-20-37	36	220	146	74	33	
			11-29-37	50	270	166	104	34	
			12-6-37	95	188	58	130	69	
			12-13-37	111	208	64	144	69	
			12-20-37	143	128	40	88	69	
			12-28-37	110	123	33	90	73	
			1-6-38	93	126	50	76	60	
			1-25-38	66	141	66	75	53	
			2-8-38	62	101	40	61	60	
61068	81	M.	12-2-37	62	246	106	140	56	Portal cirrhosis
			12-9-37	35	176	100	76	43	
			12-15-37	35	205	145	60	30	
			12-22-37	30	206	139	67	32	
			12-29-37	28	205	152	53	26	

TABLE III (Continued)

Hist. No.	Age	Sex	Date	Icterus Index	Serum Cholesterol Mg. Per 100 Cc.			Per Cent Free Choles- terol	Diagnosis and Remarks
					Total	Ester	Free		
65549	57	M.	9-21-38	250	160	12	148	92	Catarrhal jaundice
			9-28-38	201	281	85	196	70	
			10-1-38	195	290	80	210	72	
			10-10-38	100	384	160	224	59	
			10-17-38	71	286	160	126	44	
			10-24-38	52	373	160	213	57	
66041	42	F.	2-6-39	6	346	266	80	23	Portal cirrhosis
			10-27-38	34	381	163	218	56	
			11-7-38	25	528	266	266	49	
			11-14-38	40	700	424	276	39	
			11-27-38	18	794	552	242	30	
			12-2-38	11	633	457	176	27	
66047	26	M.	12-20-38	12	593	393	200	33	Catarrhal jaundice
			12-28-38	10	434	310	124	28	
			12-21-38	110	213	50	160	76	
			12-28-38	99	232	72	160	68	
			1-4-39	40	222	142	80	36	
			1-12-39	28	212	160	52	24	

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of 20 pounds in weight. Examination of the abdomen showed the liver to be palpable two fingers' breadth below the right costal border. There was no tenderness or rigidity. Temperature, pulse and respiration were normal. Important laboratory findings were: Wassermann negative; urea nitrogen 41.5; normal blood count; icterus index 250, total cholesterol 160 mg., ester 12 mg., free cholesterol 148 mg. (92 per cent), showing almost a complete absence of ester cholesterol. Bile was present in the feces. A Graham series showed a faint gallbladder shadow which was regular in outline. After a fatty meal, there was a complete disappearance of the gallbladder shadow. Patient was given routine medical treatment and a week later the icterus index dropped to 201; there was also a drop in the free cholesterol to 70 per cent, showing an improvement in the functional reserve. Four days later, the icterus index was 190 with practically no change in the cholesterol partition. Ten days later, there was a very marked drop in the icterus index to 100 and a marked decrease in the free cholesterol percentage to 59, showing further improvement both clinically and in the functional reserve. A week later, the icterus index was 71 and the percentage of free cholesterol 44. The patient left the hospital October 17, and returned a week later for follow-up, at which time the icterus index was 52, free cholesterol 57 per cent. Four months later, an examination showed that the icterus index was 6, free cholesterol 25 per cent, showing complete restoration of a normal functional reserve. At that time the urea nitrogen was 20.

COMMENT.—The question as to whether this was a medical or surgical jaundice was not definite on admission. Because of the very high percentage of free cholesterol and poor functional reserve, it was decided not to perform an exploratory operation but to treat the patient medically. Marked clinical improvement in this patient proceeded in the same ratio as improvement in the functional reserve as shown by the decreasing percentages of free cholesterol. This case illustrates very well the value of repeatedly determining the functional reserve. It should also be noted that decrease in percentages of free cholesterol is a good prognostic sign.

Case 7.—Hosp. No. 55612: A white female, age seven, was admitted to the hospital, October 19, 1937. Twice within an interval of three months, the patient had had symptoms of painless jaundice and pruritus. Examination of the abdomen revealed slight tenderness over the right upper quadrant and an enlargement of the liver five centimeters below right costal border. Stools were clay-colored; icterus index 25; total cholesterol 540 mg., ester 280, and free cholesterol 260 mg. (48 per cent), indicating a decreased functional reserve. Roentgenograms of the gallbladder showed no evidence of stones. She was extremely ill, and temperature ranged between 102° and 105° F. During the next month, the percentage of free cholesterol varied between 40 and 62, and the icterus index rose to 83. On November 20, there was a definite drop in the percentage of free cholesterol to 33, remaining at that level for a period of ten days, with the icterus index at 36. There was also an improvement in the clinical condition of the patient during this time. Immediately following the period of normal functional reserve just mentioned, the percentage of free cholesterol progressively increased reaching a high of 73, and clinically the patient became worse. This figure ranged between 53 and 60 per cent until fatal termination of the disease. The icterus index also rose, reaching a high of 143 on December 20, and decreased to 62 at the time of death. At autopsy, a perforated gangrenous gallbladder was found. A stone was found lying free in the abdominal cavity. There was a generalized peritonitis and the liver was studded with numerous small abscesses.

COMMENT.—Again, this case illustrates the value of the cholesterol partition as a guide to surgical intervention. If surgical intervention was to be



attempted in the case, the time to have operated would have been when the free cholesterol percentage had dropped to practically normal values, remaining so for about ten days. The prognostic value of the test is illustrated by our observations of this patient. The continued rise in the percentage of free cholesterol following the short period of normal functional reserve, is reflected by the poor clinical course and fatal termination.

In all of the other cases in this group, it will be noted that the initial value of the free cholesterol percentage was generally much higher than those in the other groups. After these patients had received medical treatment, it was observed that they improved, as shown by the progressive decrease in the percentage of free cholesterol. This indicated a recovery period, with improvement in the functional reserve. Accompanying this there was also a definite decrease in the icterus index. We stress the value of repeated determinations of the cholesterol partition as a prognostic aid in following the course in these patients.

*Discussion.*—It is generally accepted that disturbances of hepatic function may be reflected by changes in the cholesterol partition of the blood. Early observation of this fact was reported by Feigl,<sup>16</sup> who noted low ester cholesterol values in acute yellow atrophy. Thannhauser and Schaber<sup>8</sup> were quick to recognize and emphasize the significance of this observation. They found the ester fraction to be greatly diminished, and the free cholesterol increased in cases of severe parenchymatous hepatic diseases, and attributed this phenomenon, which they named "*Estersturz*," to a disturbance of cholesterol ester synthesis, and hydrolysis in the liver. Recently, Boyd and Connell<sup>17</sup> have indicated that lipopenia is associated with the cholesterol "*Estersturz*" in parenchymatous hepatic disease.

Opposed to the view of Thannhauser and Schaber<sup>8</sup> is that of Gardner and Gainsborough,<sup>18</sup> who state that diminution in ester cholesterol is due to impaired absorption of cholesterol and fat from the intestine in the absence of bile. Hawkins and Wright<sup>19</sup> were unable to substantiate this explanation since they have shown that the absence of bile in the intestines and faulty fat absorption in dogs with biliary fistula did not result in changes of ester to total cholesterol ratio.

Clinical evidence for and against the interpretation of the above stated opinions have been reviewed by Gardner and Gainsborough,<sup>18</sup> Epstein,<sup>20</sup> Epstein and Greenspan,<sup>21</sup> and Shay and Fieman.<sup>22</sup> Most of the investigators have tried to translate changes in the cholesterol partition into terms of liver function. It was thought to be of value in differential diagnosis between obstructive and nonobstructive jaundice. However, the general impression is that in uncomplicated parenchymatous hepatic disease, there usually occurs a diminished ester cholesterol value with a corresponding increase in the percentage of free cholesterol.

As stated by Boyd and Connell,<sup>17</sup> "the original explanation of Thannhauser and Schaber is the most reasonable one to account for the changes in cholesterol partition when damage to the hepatic cells has occurred. Cholesterol

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esters are not stored to any extent in normal tissues, although they are apparently synthesized as a by-product in degenerating tissue. A lessened production of cholesterol esters would thus soon result in a diminution in their concentration in the blood, the only medium in which they are found to any extent. Thannhauser and Schaber<sup>8</sup> have argued that since damage to the liver lowers the cholesterol fraction in the blood, it is likely that these substances are produced in the liver. Supporting this is the fact that cholesterol esterases have been found in the liver."

Previous investigators, reporting on the estimation of the cholesterol partition, have utilized methods which we believe are not so accurate as those of recent origin. By the newer procedures the free cholesterol in normal individuals generally is not greater than 30 per cent of the total cholesterol as against variations of 30 to 50 per cent, which were formerly considered as normal. Refinement in technical procedures has resulted in better evaluation of the observations thus obtained and in better clinical interpretation.

We have utilized the changes in the cholesterol partition of the blood serum as a measure of the functional reserve of the liver and have presented evidence to show that this interpretation is of value to the surgeon. This value lies in an indication as to the most opportune time for surgical intervention in disease involving the gallbladder and biliary tract. This fact is amply demonstrated by the data given in Table I. Actually, all of these patients, with the exception of No. 39365, who died of a pulmonary embolism, did well postoperatively. Further evidence that the functional reserve plays a rôle in the ability of the patient to withstand operation, is shown by the four cases in which the initial functional reserve was diminished, and who received medical preoperative treatment, which resulted in restoration of this reserve. We are of the opinion that if these patients had been operated upon during the period of decreased functional reserve, their postoperative course would have been poor.

Further, patients operated upon in whom the cholesterol partition revealed a lowered functional reserve, as shown by observations recorded in Table II, all had a stormy postoperative course. Several terminated fatally. The third patient of the group, No. 55111, underwent two operations; previous to and during the first postoperative period, this patient had a low functional reserve as shown by the increased percentage of free cholesterol. With improvement in the reserve there was also marked improvement in the clinical condition. At the time the second biliary tract operation was performed, her functional reserve was considered normal, and the postoperative course, in contrast with the previous one, was uneventful. This particular case illustrates that the information obtained from the determination of the cholesterol partition is of definite prognostic value.

### CONCLUSIONS

Determination of the cholesterol partition of the blood serum, particularly the changes in the percentage of free cholesterol, has been used as a measure of the functional reserve of the liver.

A patient who exhibits a low functional reserve of the liver is a poor operative risk. Medical treatment should be instituted, and repeated estimations of the cholesterol partition will indicate when the functional reserve has returned to normal. Such information is of value as a guide to surgical intervention.

The cholesterol partition has prognostic value in surgery of the gallbladder and biliary tract.

We suggest that the cholesterol partition of the blood serum be determined both pre- and postoperatively in all patients with biliary disease and jaundice.

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*Discussion.*—DR. JOHN A. WOLFER (Chicago): The subject presented by Doctor Pickhardt is one that I have been interested in for some time, and I think all of you have been interested in the matter of the liver as a very essential factor in biliary tract surgery. The physiologists tell us that, so far as they know now, the liver may have approximately 22 functions and probably there may be a few zeros added to that in the course of time. Therefore, it is extremely interesting, and probably pertinent, to realize that there is no one function test of the liver. As to whether isolated portions of the liver or specific liver cells perform certain functions there is a question. I am inclined to feel that there is a considerable overlapping of liver anatomy with liver function.

I should like to present three charts which will indicate the value of establishing the blood cholesterol partition, to see how it compares with conditions as we meet them.

CHART I

F. K., male, age 55. Entered hospital August 29, 1938.

Pain in the abdomen and jaundice of 8 days' duration. Clay-colored stools.

Mass in the right upper abdomen which varied in size. Loss of weight.

Operated upon September 9, 1938, cholecystduodenostomy.

Diagnosis: Carcinoma of the head of the pancreas with liver metastases.

Autopsy: October 20, 1938. Diagnosis verified. 4000 Gm. of carcinoma in the liver.

Date	Cholesterol				Plasma Protein			Blood Sugar	Ict. Ind.	Ser. Bili.	N.P.N.	B.U.N.
	Total	Ester	Free	%	Total	Alb.	Glob.					
8-30-38.....	255	140	115	45	6.8	4.4	2.4	109	91	11.7	34.5	15.7
9-1-38.....	251	133	118	45					93	12.1		
9-9-38.....					Cholecystduodenostomy							
9-12-38.....	186	97	89	48	6.3	3.38	2.92		50	5.9	28.3	12.0
9-16-38.....	180	109	71	33	6.3	3.37	2.93		40	2.6		13.4
9-23-38.....	207	140	67	32	6.3	3.38	2.92		25	1.0	27.3	12.3
9-30-38.....	205	138	67	32	6.5	3.34	3.16		20	1.0		
10-10-38.....	177	104	73	41	6.9	3.38	3.52		17			
10-14-38.....	152	86	43	43	7.0	3.42	3.58		17			
10-20-38.....					Expired							

Chart I is from the study of a male, who had pain in the right abdomen, jaundice for eight days' duration, clay-colored stools, and a mass in the right upper abdomen which fluctuated in size from time to time. There was a loss of weight. He was operated upon and a carcinoma of the head of the pancreas was found with metastases in the liver. A cholecystduodenostomy was performed September 9, 1938. The man died in October and the diagnosis was verified, there being found approximately 4,000 Gm. of carcinoma in the liver. Here we have a case with a high grade biliary obstruction which was relieved by operation with a residue of extensive carcinoma of the liver. You

will note that the original cholesterol study revealed 45 per cent free cholesterol and normal plasma proteins. We are studying the plasma protein albumin-globulin ratio as a parallel with the cholesterol partition, on the assumption that esterification of cholesterol and the formation of protein fractions occur in the liver. The blood sugar was normal, the icterus index 91 and 92, serum bilirubin 11 and 12, and the blood urea nitrogen and nonprotein nitrogen not elevated. Following operation, there was an immediate rise in the free cholesterol to 48 per cent, but after a few days there was a distinct fall to 32 per cent. During this time there was a marked drop in the icterus index and serum bilirubin, as was to be expected. Due to drainage, however, a little later, ten days before death, the percentage of free cholesterol again began to increase. It is also interesting to note that during the terminal two weeks there appeared an inversion of the albumin-globulin ratio of the plasma protein—albumin 3.42 and globulin 3.58. Also, there is shown that the icterus index has fallen to 17 and the serum bilirubin to 1.0. In my opinion this chart clearly demonstrates and verifies Doctor Pickhardt's theory. The high percentage of free cholesterol was the result of liver damage. There was some

## CHART II

L. G., male, age 52, February 3, 1939.

For 3 weeks malaise, anorexia and abdominal discomfort. Jaundice for 4 days.

Highly colored urine for 10 days. Long history of sinus infection. Jaundice deepened with marked itching of the skin. Some low grade fever. Low blood pressure.

Diagnosis: Diffuse hepatitis with cirrhosis. Ascending cholangitis.

Date	Cholesterol				Plasma Protein			Blood Sugar	Ict. Ind.	Serum Bili.	N.P.N.	B.U.N.	Proth. Time	Ser. Phos.
	Total	Ester	Free	%	Total	Alb.	Glob.							
2-4-39...									200					
2-11-39...									240				50.8	
2-17-39...									250				40.5	
2-22-39... 278	645	213.5	77.8										35.7	
2-24-39...									250				34.8	
2-28-39... 157	387	148.3	79.3	5.53	3.68	1.85						12.9	32.9	
3- 2-39...	Drainage of Gallbladder													
3- 6-39...									150	40.2			32.4	
3-17-39... 238	174	64.0	26.9	6.05	4.14	1.94			50	4.5	30.6	13.3		7.0
3-18-39...	Tube Out													
4-11-39... 281	195	86.0	30.3	6.80	4.59	2.21	86	50	1.0	39.4	18.2		3.3	

immediate relief by drainage, as expressed by a decrease in free cholesterol, however, because of the extensive liver damage due to carcinoma the relief was only temporary, to be followed by increasing percentages of free cholesterol and inversion of the albumin-globulin ratio of the plasma proteins.

Chart II is from the study of a male, age 52. There was a history of approximately three weeks of increasing weakness, anorexia and abdominal discomfort. Jaundice appeared about four days before admission to hospital, and itching of the skin, which had been present for some days, became progressively worse. The first cholesterol study revealed 77 per cent free, and a few days later it had risen to 79.3 per cent. The icterus index on first study was 200 and rose to 240 and finally to 250. The prothrombin time, based upon a standard of 20 seconds as normal, was 50.8 seconds. In spite of active treatment with large amounts of viosterol and calcium, a high sugar intake with vitamin K and bile salts, the symptoms became more acute. The prothrombin time had dropped to 32.9 seconds, however, but the percentage of free cholesterol had risen to 79.3 per cent as previously mentioned. He was operated upon two days after the last mentioned blood chemistry work. At exploration, the liver was found to be hard, retracted and mottled. The ducts were



# THE CHOLESTEROL PARTITION

not dilated but were gray in color and the walls thickened. Because of the poor reaction of the patient, a solitary small stone was removed from the gallbladder and the viscus was drained. The contents consisted of a clear yellow fluid. It will be noted that after an uneventful postoperative course of approximately two weeks, the free cholesterol had dropped to 26.9 per cent, which can be considered normal, the icterus index to 50 units, and, 40 days after operation, the free cholesterol was 30.3 per cent, and the serum bilirubin 1.0. In this instance, the clinical improvement of the patient closely paralleled the improvement or return to normal of the percentage of free cholesterol.

## CHART III

G. K., male, age 46, March 10, 1939.

In March, 1938, noted jaundice, pain in right side of abdomen, and weakness. Occasional vomiting. In July, 1938, reported at Clinic. Marked jaundice and loss of weight. Large abdominal tumor believed to be liver. Wassermann positive.

Diagnosis: Malignant disease. Put on antiluetic treatment and improved very materially but liver did not decrease in size. Explored March 15, 1939.

Diagnosis: Extensive amyloid disease of the liver.

Date	Cholesterol				Plasma Protein			Blood Sugar	Ict. Ind.	Serum Bili.	N.P.N.	B.U.N.	Proth. Time	Ser. Phos.
	Total	Ester	Free	%	Total	Alb.	Glob.							
3-13-39...	334	180	153	46	6.50	4.01	2.58	80.4	30	1.5	20.5	12.5	32.75	47.78
3-14-39...					60% clearance—Hippuric Acid									
3-15-39...					Exploration—Biopsy from Liver									
3-17-39...					7.60	4.75	2.40			.45			81.85	
3-24-39...													30.35	
3-28-39...	248	103.5	144.5	58	5.86	3.74	2.12	79.5	55	6.5	21.7	9.55	22.00	23.08
4-7-39...	212	97.5	114.5	54	5.40	3.16	2.24		30	2.3	44.2	27.8	24.00	33.5
4-21-39...	368	96.0	272.0	74	7.60	4.50	3.10	82.0	50	2.72	27.3	12.0	20.2	137.0
4-26-39...	417	122.0	295.0	71	7.40	4.55	2.85	86.6	40	1.5	30.0	12.5	19.1	94.0
4-27-39...					69.4% Clearance—Hippuric Acid									

The observations shown in Chart III were made on a case of proven extensive amyloid disease of the liver. Preoperatively, the free blood cholesterol was 46 per cent, there was a normal albumin-globulin ratio of the blood plasma protein, the prothrombin time was 32.75 seconds, and the serum phosphatase was 47.7 units. The hippuric acid test showed 60 per cent clearance. The operation consisted of an exploration with removal of a small piece of the liver for microscopic study. Two days after operation, the prothrombin time was 81.85 seconds (normal 21 seconds), he began bleeding from the wound, there was evidence of subcutaneous hemorrhage and his condition became critical. He was given "klotogen" and bile salts through a duodenal tube, and because of severe dyspnea, oxygen was administered. A week later, the prothrombin time had fallen to 30 seconds and bleeding had practically ceased. Two weeks after the exploration, the free cholesterol was 58 per cent and the serum phosphatase 23 units. It will be noted that 37 days after operation the free cholesterol was 74 per cent, the albumin-globulin ratio practically normal, the icterus index 50, the prothrombin time 19 seconds, and the serum phosphatase 137 units. At this time, he was feeling quite well. However, it is quite evident that he has extensive liver crippling because of the diffuse amyloid disease, and this is demonstrated by an increasing free cholesterol and serum phosphatase. Nevertheless, one function of his liver had adjusted itself—that which deals with blood clotting as evidenced by a normal prothrombin time and cessation of bleeding.

I feel, as does Doctor Pickhardt, that in the study of blood cholesterol partition we have at our disposal one test which will aid us in formulating an

opinion relative to the condition of the liver, and will act as one guide as to when surgical interference may be carried out with relative safety.

DR. ROBERT L. PAYNE (Norfolk, Va.): This presentation by Doctor Pickhardt seems to me to corroborate what we have observed over a period of about five or six years now and followed in our biliary surgery; namely, Epstein's work, which practically correlates the presentation he has made to-day, that is, the high total cholesterols and the low esters.

I noticed in all of the charts, of both Doctor Pickhardt and Doctor Wolfer, that in those cases that showed a marked liver dysfunction, the cholesterols were high and the esters low, and that is the point Epstein so ably brought out and emphasized in numerous articles.

As Doctor Wolfer aptly said, there are too many functions to the liver for any one liver test to be of great value, but I think if one is getting any help out of anything that he is doing, he at least ought to express it, and we have been getting a great deal of comfort for about three or four years now out of determinations of xanthoprotein and blood indican in suspected and determined liver dysfunction. This is based on the fact that physiologists tell us that the indol group is broken up in the liver through a mechanism in which ether sulphuric acid breaks up the indol into xanthoprotein and indican. Where this mechanism is disturbed, this does not take place, and in the blood you find an increase of xanthoprotein and a lowering of blood indican, which is just exactly the reverse of an Epstein lipoid nephrosis in which the xanthoprotein is increased and the blood indican is increased.

In those gallbladder cases where we have drained the common duct or where there is a biliary fistula, we have, in addition, been getting a great deal of comfort out of the study of the chlorides of the bile excreted.

We have noted that where there is an impending liver dysfunction the bile chlorides will rise and with an improvement in the liver condition the chlorides will fall. Correspondingly, with this bile study we have carried Epstein's work out on the total cholesterols and the esters and we have found that although Epstein prognosticates the definite improvement when the ester relationship to the totals approach normal, yet it is a slower process than the determination of the chlorides in the bile. In other words, we make out in a daily chemical examination of the bile that a falling chloride, approaching normal, will indicate a return of the liver to its normal function two or three days sooner than the cholesterol estimations according to the Epstein method.

DR. OTTO C. PICKHARDT (closing): I did not know that Doctor Wolfer was working on this problem until he wrote me about it, and I was much interested to hear that his results were very much in line with ours.

This test does not indicate the type of liver damage, that is, one can get a low functional reserve in such various conditions as: Cholelithiasis, carcinoma, catarrhal jaundice, hepatitis and chronic passive congestion. Therefore, we do not want it thought that we have used this test for a differential diagnosis—we have not!

Doctor Payne's remarks on Epstein's work are correct, of course, but the difference in Epstein's and our work is that we have particularly stressed the percentage of free cholesterol instead of the ester cholesterol, since it has been shown that the percentage of free cholesterol is a physiologic constant in the normal individual. On the other hand, work in our laboratory has shown that along with the cholesterol esters there may be included a substance which is not entirely cholesterol ester and we believe that changes in the percentage of free cholesterol is a much better criterion. We are not as yet ready to report upon this undetermined substance.

## GANGRENE OF THE EXTREMITY IN THE DIABETIC\*

ARTHUR A. ZIEROLD, M.D.

MINNEAPOLIS, MINN.

GANGRENE of the extremity in the diabetic manifests itself in two forms. The uncomplicated ischemic necrosis typical of the nondiabetic arteriosclerotic, commonly termed "dry gangrene" and the septic necrosis known as "moist gangrene."

The latter condition, which is the subject of this discussion, is not the result of a sudden vascular occlusion but is the culmination of a series of changes. Slowly, progressive intimal thickening permits the development of collateral circulation until eventually a delicate balance between life and death of the tissue is reached. When gangrene occurs it is more often the result of increased demands of the tissue cells due to the metabolic disturbances of sepsis and diabetes than to an immediate decrease in blood supply. Local bacterial invasion initiates or attends the development of this process, and soon becomes the dominating factor. The combination of sepsis and persistent but inadequate blood supply results in a moist spreading gangrene which untreated or unchecked causes death. If by way of treatment, early amputation is undertaken, it must be at a level which precludes further spread of the process or reoperation. This entails high amputation with its risk to life and the loss of excessive amounts of good tissue. If amputation is undertaken late in the progress of spreading gangrene, the mortality rate is high, due to the combined effect of sepsis and diabetes. If, however, it be kept in mind that gangrene occurs not because of suddenly diminished blood supply to the part but because of suddenly increased cell needs and that if the tissue metabolism be returned to normal or nearly normal the blood supply would again be adequate, the necessity for amputation as the primary therapeutic procedure becomes less apparent. On the basis of this concept, it would appear reasonable that, in the presence of a spreading gangrene, if infection be eliminated, the diabetes could be controlled, and that if the diabetes with its disturbed metabolic processes and abnormal cell needs be controlled, gangrene would not recur.

Upon this assumption has been developed the following method of treatment which has obtained at the Minneapolis General Hospital during the past five years:

Upon admission to the surgical service with a spreading gangrene, the status of the patient's diabetes is determined, together with the incidental observations of ketosis, nitrogen balance, blood concentration and signs of dehydration. Normal hemoglobin and plasma protein levels are then restored by multiple transfusions and normal fluid balance is established—preferably by mouth or bowel. No great effort is made to control blood sugar levels

\*Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

at this time, as in the presence of infection control of blood sugar levels and the products of abnormal metabolism is difficult and at times impossible. At the end of a 24-hour period, attention is directed to the local sepsis and gangrene. Under pentothal anesthesia, all infected or devitalized tissue is removed, together with any exposed bone. Contrary to the usual débridement, no attempt is made to save important structures, the goal being a base of live tissue with no gross evidence of infection and no pockets or overhanging skin borders. The wound is then covered with cod liver oil dressing and 12 to 24 hours later the patient is placed in a chair with the affected leg dependent and immersed to midcalf in 3 per cent saline at 100° F. The bath is alternated with bed rest at hourly intervals during the day. With the control of sepsis and diabetes, the gangrene is arrested and several days may be devoted to improving the patient's general condition. When the patient's temperature has remained at a normal level for three days, amputation may be undertaken as an elective procedure.

During the past five years, the mortality due to gangrene in the diabetic at the Minneapolis General Hospital has sharply decreased and we have come to accept the following doctrine:

(1) In the presence of sepsis and spreading gangrene, amputation should not be considered as a primary therapeutic measure.

(2) Amputation should be undertaken only as an elective operation, never as an emergency.

Of 92 cases treated during 1937 and 1938, 68 were treated by preliminary débridement and later by major amputation. Of these, eight or 11.7 per cent, died from pneumonia or coronary disease. None developed local infection and none necessitated reoperation following amputation. Twenty-four cases were treated by preliminary local excision with one death from bacteremia. Twelve refused later amputation and were discharged against advice. Others were discharged for a trial period. Of the entire group, the mortality was 9.7 per cent. Of the major amputations, 11.7 per cent, and of the preliminary excisions, 4.1 per cent.

At the University of Minnesota, where this procedure has been adopted during the past year, the amputation mortality has been decreased from 50 to 10 per cent.

DISCUSSION.—DR. WILLIAM E. GALLIE (Toronto, Canada): I wish to congratulate Doctor Zierold on his important and excellent presentation and to emphasize some of the points that he has made.

Soon after the discovery of insulin we adopted the policy of placing all the surgical diabetics under the care of one man, in order that we might determine as quickly as possible whether the new medical treatment would influence the surgical complications. As a result, Dr. W. G. Murray has rapidly acquired a wide experience in the disease and has made important observations which agree in principle with those enumerated to-day by Doctor Zierold.

The outstanding result of the ten-years study has been that with adequate medical care one may confidently expect a great reduction of the mortality rate in so-called diabetic gangrene and also a great saving of limbs. Whereas,

## DIABETIC GANGRENE

formerly high amputation was performed at once in most cases of serious infection in the feet, the practice now is to control the diabetes with insulin and glucose and to treat the infection by wide incision and adequate drainage. The result is that in many cases the infection is controlled and the wounds ultimately heal.

In the more serious cases of spreading, moist gangrene our practice differs from Doctor Zierold's in that instead of a local operation on the infected gangrenous area we perform an immediate guillotine amputation about the middle of the calf, leaving the wound wide open for drainage. In a whole series of cases, this has resulted in immediate control of the infection and has allowed a subsequent formal amputation at a higher level without the risk that would attend such an operation at the height of the infective process. This, however, does not differ in principle from the method described by Doctor Zierold and I mention it only to emphasize what he has said.

DR. LELAND S. MCKITTRICK (Boston): When I read Doctor Zierold's abstract in our printed program, I was quite distressed because I could not but feel that Doctor Zierold and I had very little in common in the management of this group of cases. After talking with him yesterday and after hearing his paper to-day, however, I would like to add my commendation to that of Doctor Gallie on what he has accomplished.

TABLE I

DEATH AFTER OPERATION UPON LOWER EXTREMITIES—806 PATIENTS

Cause	No. Cases	Per Cent	
		of Deaths	of All Patients
Infection . . . . .	42	50	5.2
Cardiorenal (including pulmonary embolus)	37	44	4.6
Miscellaneous . . . . .	5	6	0.6
Total . . . . .	84	100	10.4

DEATH IN NONOPERATIVE TREATMENT OF LOWER EXTREMITIES

No. Patients . . . 273      Deaths . . . 12      Mortality . . . 4.4 per cent

I think we all feel, as Doctor Gallie does, that it is of fundamental importance to distinguish between the group of cases whose arterial circulation is adequate and that more serious group where it is not. In this discussion I am limiting myself to the group of patients with inadequate circulation, and I think it is this group of patients that Doctor Zierold has been talking about.

Doctor Zierold has faced a serious problem that is not as uncommon as we might think. There is in the recent literature a summary of hospital mortality in which 12 hospital services in this country are listed. Eighteen to 75 per cent of these patients have died following amputations for gangrene. In eight of those 12 hospitals the mortality was over 50 per cent and in only one of them was it under 30 per cent.

As with Doctor Gallie, we have met this problem in a somewhat different way than Doctor Zierold, possibly because many of us in Boston who have been interested in this group of cases have not had to face a 60 per cent mortality. One of our former presidents, Dr. D. F. Jones, succeeded in bringing that 60 per cent mortality down to about 20 per cent before we were anything more than embryonic surgeons.



I should like to show a few statistics from which I will try to demonstrate certain facts which have influenced us in the management of these cases.

In Table I are grouped the causes of death in all of the patients whose lower extremities we have operated upon. The mortality in this group is 10.4 per cent. About one-half of these died from infection. Four point six per cent, or roughly 5 per cent, of the patients operated upon have died from some form of cardiovascular disease. Interestingly enough, about one-half of our patients are not operated upon, and the mortality in this group is also about 5 per cent. This 5 per cent, then, is the irreducible minimum that Doctor Zierold has mentioned. We believe, however, that the mortality rate in excess of this figure for the most part due to late, inadequate, or improper treatment.

TABLE II

## FIRST 100 AMPUTATIONS FOR DIABETIC GANGRENE

Dead.....	92
Living.....	8
Living 3 years.....	58%
Living 5 years.....	35%
Average duration of life (92 patients)	42.7 months.

Table II presents another phase of the problem: Of the first 100 patients who left the hospital following amputation for gangrene, eight are still alive. However, one-half of the patients were already dead at the end of three years and at the end of five years only one out of three patients was alive. The average length of life after operation in the 92 dead patients was three and one-half years. In other words, the diabetic patient with gangrene looks forward after amputation to an average life expectancy of only three and one-half years. We must, therefore, be careful in whatever we plan not to have them spend too much of this time within the hospital walls.

TABLE III

## TYPE OF AMPUTATION IN 503 PATIENTS WITH DIABETIC GANGRENE

Level	Cases	Per Cent of Total	Deaths	Mortality Per Cent
Toe.....	53	10.5	4	7.5
Toe then major oper.....	35	7.0	4	11.4
Lower leg.....	36	7.2	1	2.8
Guillotine.....	33	6.6	14	42.4
Gritti-Stokes.....	80	15.9	11	13.8
Thigh.....	266	52.9	31	11.7
Totals.....	503		65	12.9

Table III shows the type of operations performed upon 503 diabetic patients with gangrene from 1923 to 1938. I should like to call your attention to the 33 patients (7 per cent of the group) who have had a guillotine amputation. In other words, in the group of patients that we see who are in need of an amputation but whose general condition is so poor or whose local infection is so extensive as to contraindicate primary closure, we would not undertake the local procedure that Doctor Zierold advises, but instead a guillotine amputation through the upper third of the lower leg, planning to follow this by a higher amputation at a later date.

There is one other point that I should like to make. Interestingly enough,

there is no agreement among surgeons, at the present time, as to what represents the safest, surest, and simplest closed amputation for a diabetic patient who is such a poor risk that one can be confident that he will never use an artificial limb. You will notice in Table III that approximately half of our patients have a primary, closed supracondylar amputation, with a mortality of 11.7 per cent. This operation has been elected because it represents the amputation which, in our hands, is followed by the highest incidence of healing *per primam* and the shortest period of hospitalization.

DR. FRANK L. MELENEY (New York, N. Y.): In this condition, we are dealing with a problem of infection, and that concerns bacteria. I have been surprised that Doctor Zierold did not make any mention of the bacteriology of these infections, because I think that that is one of the fundamental bases upon which the form of treatment in any given case must be determined. Here we have a condition in which there are a number of important organisms which are responsible for death, and it is essential, it seems to me, for the surgeon to know with what organisms he has to deal before instituting treatment.

Anaerobic bacteriology is particularly applicable here, because the Welch bacillus and the anaerobic streptococci are particularly common. Also, in this condition, we have the factor of bacterial symbiosis or synergism. In diabetic gangrene, there is almost always a mixture of organisms, and I believe that those organisms working together make the infection infinitely more virulent than it would be if any of the organisms were to be found in pure culture. In some cases in which gas gangrene or some other overwhelming infection is present when the patient is admitted, a quick guillotine operation is indicated without waiting for bacterial cultures. However, in most cases time is afforded to make a complete analysis of the bacterial flora.

We are making it a routine procedure to establish, as soon as possible, the number and kind of organisms that are present in all cases of diabetic gangrene. During that time, the preliminary preparation of the patient, from the point of view of the diabetes, can be carried out. Cultures should be taken not from one place but from many places in the gangrenous area. Thus, all of the organisms with which one has to deal can be determined. Of course, all of the organisms which can be found on the surface are not necessarily important. Many of these may not have invaded the tissues deeply, but certainly there is no organism which is deep which cannot be found on the surface. If the hemolytic streptococcus or the Welch bacillus or any of the anaerobic streptococci are known to be present, then the possibility of their later developing an infection at the site of amputation should be in the mind of the surgeon. He will anticipate it, be ready for it, and, if possible, prevent it. To be forewarned is to be forearmed. No one should be surprised if gas gangrene develops in an amputation stump.

Also, if cultures are taken at the time of, and at the site of amputation, the surgeon may know what organisms to expect if an infection develops there secondarily. It seems to me to be reasonable to plan on an open amputation if the Welch bacillus, if the hemolytic streptococcus, or if any of the microaerophilic or anaerobic streptococci are found in the original gangrene. Secondary closure can then be performed at the site of amputation, if cultures taken at the time of amputation show no evidence of the presence of those organisms after 24, 48, or 72 hours, and the wound can be prepared to be closed in that time with the expectation of primary healing. If those organisms are not present in the original gangrene, the surgeon can close his amputation with much more feeling of satisfaction and equanimity and with

every expectation that his wound will heal without subsequent infection. The level of amputation should depend largely upon the level of adequate circulation.

The *Staphylococcus aureus* is another organism which may invade, and if present, the surgeon should know that there is a possibility of its invasion. If he closes the wound at the primary amputation, then he must be particularly careful to observe the earliest signs of inflammation. If infection develops in the wound which he has closed, then he should open it and treat it specifically if he knows the organism which is likely to be present.

Zinc peroxide is often of service in these cases. It may be employed to hold the local lesion *in statu quo* while the general diabetic condition of the patient is being brought under control. Later, if the Welch bacillus or the anaerobic streptococcus or the hemolytic streptococcus is found to be present at the site of amputation, zinc peroxide should be used for immediate and specific treatment.

In short, we have here a complicated problem with three major factors: diabetes, blocked arteries and infection. All of these factors must be given serious consideration if we are going to reduce the mortality in these cases to a reasonable figure.

DR. HERMAN E. PEARSE (Rochester, N. Y.): As with Doctor McKittrick and Doctor Gallie, we have approached the problem in a little different manner. If there is any difference, it would appear to be more apparent than real due to confusion in terminology. For this reason I would like to make a plea to abandon the term "diabetic gangrene." It covers a multitude of conditions which are not treated alike. In fact, the management of these cases is predicated not on the diabetes nor on the gangrene, but on the state of the circulation.

You all know that under the term "diabetic gangrene" are included such diverse conditions as dry, senile gangrene, and the gangrene from thrombosis or infection in the presence of an extremely good circulation. In the first instance, local surgery is apt to be dangerous. In the latter instance, local surgery is obligatory, because with a good circulation, local operation will frequently cure the individual and avoid an amputation. In between these two extremes there are all varieties of combination of infection and circulatory deficit. Unfortunately, one cannot say quantitatively how much the circulation is impaired. It would clarify this situation greatly if we might determine that an individual has a 30 per cent deficit or an 80 per cent deficit in his circulation, then we would use a uniform nomenclature.

It would appear desirable, then, not to include all cases under the one term of "diabetic gangrene." If this is done, we can segregate the patients that would profit by local measures. I am sure the greatest hope for the individual who has gangrene with a competent circulation is in the local surgery which avoids loss of the limb.

DR. ALTON OCHSNER (New Orleans, La.): We have been able to decrease the mortality rate in these cases in our institution by having them under the care of one man, Doctor Charbonnet, who, because of his preliminary training in internal medicine, is particularly able to handle them effectively. We have divided the cases of diabetic gangrene into three groups: One, in which there is a progressive gangrene associated with infection; another, in which there is considerable vascular competence; and the third, in which there is no vascular competence and in which the infection is mild. In the first group, we are convinced that early amputation is life-saving as

# DIABETIC GANGRENE

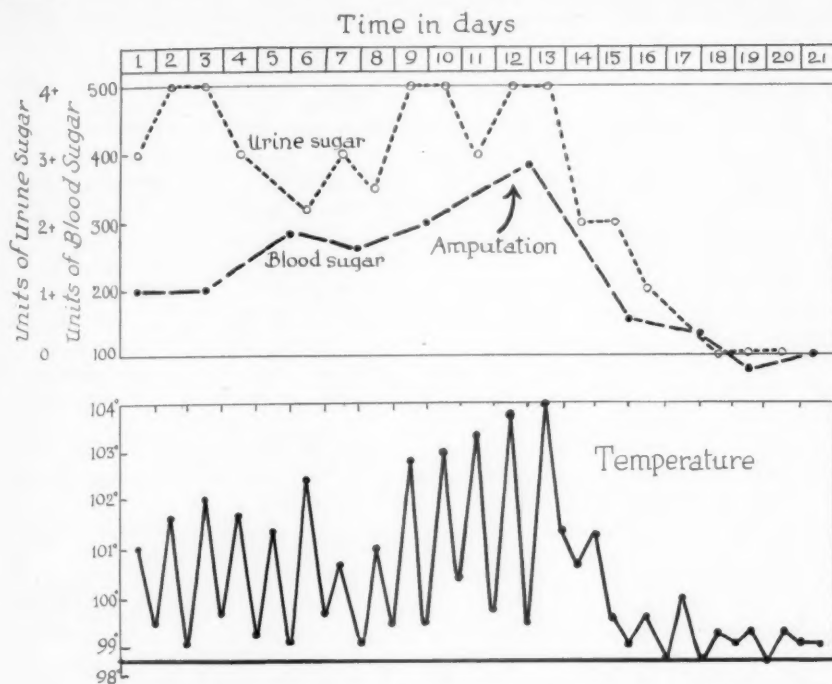


CHART 1.—Clinical course of a case of diabetic gangrene in which conservative therapy was employed, showing persistence of hyperglycemia, glycosuria, and fever in spite of attempts to control the diabetes. Shortly after removal of the infected gangrenous foot, temperature, blood sugar, and urinary findings became normal.

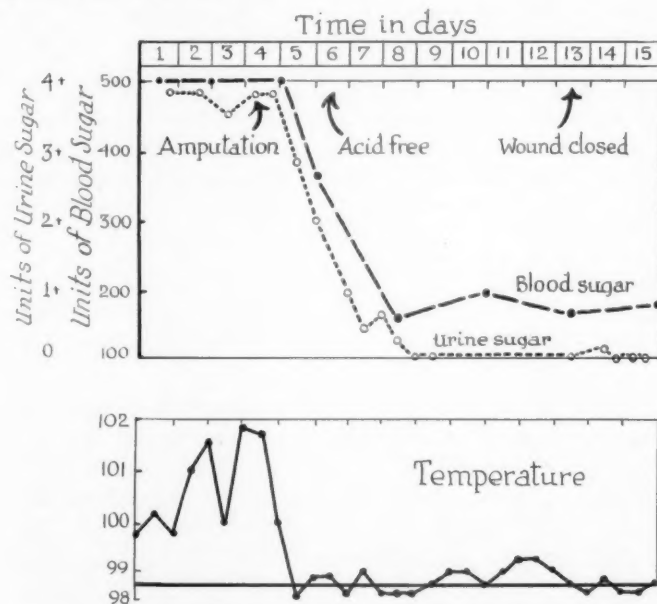


CHART 2.—Clinical course of severe diabetic gangrene, illustrating the prompt return to normal of temperature, blood sugar, and urinary findings immediately after amputation. The diabetes in this case was much more severe than that illustrated in Chart 1, although the decrease in symptoms was very prompt following removal of the infected foot.

illustrated by the two cases whose clinical course is presented in Charts 1 and 2.

I would like to discuss the second group of cases to which Doctor Pearse has already referred.

Contrary to what is commonly thought, the patient whose peripheral pulsations are absent need not necessarily have an incompetent vascularity. I think we as surgeons pay too little attention to the possibility of a vasospastic influence originating in an infected focus in an extremity. Because of this, in these patients in whom there is not the urgency for amputation we have done a novocain block of their lumbar sympathetic ganglia and studied by means of plethysmographic determinations the pulsations of the arterioles of the toe, and in this way determined the degree of vascular competence.

In those cases in which there was a considerable vascular competence, in spite of the fact that there may be obliteration of the larger vessels, as evidenced by absence of pulsation, we have felt ultraconservatism was justified. Following the determination of vascular competence by means of novocain block, the sympathetic ganglia are blocked with alcohol which produces vasodilatation for six to eight months.

I feel if one will consider the possibility of vasospasm in these patients in whom there is a necrosis or infection and offset the vasospasm by first novocain block and later alcohol block of the sympathetic ganglia, the possibility of saving these extremities and getting a good extremity can be greatly enhanced.

DR. ARTHUR A. ZIEROLD (closing): It is interesting in traveling to look around and see how many have arrived at the same destination but by different routes. I feel a certain sense of gratification in that Doctors Gallie, McKittrick, and Ochsner have arrived at approximately the same destination, although by different routes.

There is little that I can add to the discussion other than to recall one statement, and that is that we are not concerned solely with an alteration in blood supply, but we are concerned in an alteration in the cell needs and the cell metabolism.

As to the efficacy of the different procedures, I perhaps neglected to intimate that this was in my mind, namely, *a* method of treatment of gangrene in the diabetic, and not *the* method. I appreciate very much the manner in which you have received this communication.



## FIBROMA OF THE OVARY WITH ASCITES AND HYDROTHORAX\*

### A FURTHER REPORT

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SINCE the first report of this syndrome by Meigs and Cass,<sup>10</sup> in 1937, two articles have added three recent cases. One case has recently been reported in full by Rhoads and Terrell,<sup>12</sup> and two others are recorded by Weld.<sup>18</sup> A further search in the literature, stimulated by a paper of Dr. Muriel B. McIlrath,<sup>8</sup> in 1937, has brought to light two much older cases. A case reported by Dr. U. J. Salmon,<sup>14</sup> in 1934, is of the same nature. Recently, Dr. Richard H. Miller<sup>11</sup> and Dr. Donald Macomber<sup>7</sup> have each operated upon a patient with this entity. These additions to the report of Meigs and Cass bring the recorded cases to 15. Thus it is clearly established that this condition is a definite entity and deserves to be called a syndrome. The reason for the fluid in the chest as well as the abdomen is no clearer and even the availability of an autopsied case fails to throw light on the problem.

The importance of this syndrome is great, for unexplained pleurisy and ascites may be caused by a tumor that can be overlooked even on careful examination. Abdominal paracentesis may be necessary before the ovarian tumor can be felt. The case of Rhoads and Terrell (No. 15) demonstrates how easily a patient could be allowed to die with a diagnosis of inoperable malignancy. It is certain that if 15 cases have been found there must be many others, especially as six of the 15 have been operated upon by members of the Massachusetts General Hospital Staff. It is certain, therefore, that throughout the world many patients with this curable lesion have been doomed to a slow death.

In patients with abdominal tumors and fluid in the chest it is very important that the chest be tapped and roentgenograms then taken. These may show, as they did in Case 10, that when the fluid was removed no evidence of metastatic malignancy was found. If such roentgenologic study, plus examination of the patient after abdominal paracentesis, could be made a routine, then other unrecognized cases would be separated from the group of metastatic malignancies.

In no text-book on gynecology or pathology has there been definite mention of fluid in the chest being found in conjunction with fibroma of the ovary. Fluid in the abdomen is mentioned many times, but not fluid in the chest. In articles by Hoon,<sup>4</sup> McIlrath,<sup>8</sup> Rhoads and Terrell,<sup>12</sup> Weld,<sup>18</sup> and in my<sup>9</sup> own book on pelvic tumors, the presence of chest fluid is described. Cullingworth's<sup>1</sup> case, reported in 1879, is the first description of this interesting entity. His patient died, and the autopsy does not explain how the fluid traveled from the abdomen to the chest, a question that is important to solve.

\* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

*Symptomatology.*—The most frequent symptoms of this lesion are difficulty in breathing and a sense of pressure and weight in the abdomen. Most patients had dyspnea, some over long periods of time (months). The presence of ascites, or at least of an abdominal mass, was known to have existed in one case (Case 15) for eight years and in another (Case 1) for five years. Table I shows that abdominal symptoms may be of long or short duration. A number of patients complained of abnormal bleeding—an evidence of failing ovarian function. Small ovarian cysts in normal or tumorous ovaries may be considered such evidence. These cysts, follicle in type microscopically, resemble those seen in other solid tumors of the ovary such as Krukenberg tumors; and in the latter cases abnormal bleeding may be present. As in metropathia hemorrhagica, failing ovarian function is manifest by a persistent follicle cyst. Symptoms of dyspnea, pain and discomfort in the chest, and the presence of abdominal distention should draw attention to this lesion.

TABLE I

DURATION OF KNOWLEDGE OF ABDOMINAL MASS OR DURATION OF ABDOMINAL SYMPTOMS			
Case 1.....	5 years	Case 8.....	1 year
Case 2.....	3 years	Case 9.....	3 months
Case 3.....	2 weeks	Case 10.....	3 months
Case 4.....	1 year	Case 11.....	Several years
Case 5.....	1 year	Case 12.....	2 months
Case 6.....	3 years	Case 13.....	6 weeks
Case 7.....	At admission	Case 14.....	2 years
Case 15.....	8 years		

*Physical Examination.*—Physical or roentgenologic examination disclosed the presence of fluid in the chest in every case. In some it was only demonstrated roentgenologically, but in 12 cases it was demonstrated by tapping the chest and obtaining fluid. In only six was the abdomen tapped to prove the presence of fluid, but at operation, abdominal fluid was found in all cases. In all patients, but in some only following abdominal paracentesis, a mass was found in the abdomen. Cachexia is not uncommon and is due to rapid dehydration because of the quick reaccumulation of fluid in the chest and abdomen after tapping.

*Laboratory Data.*—The laboratory findings in subsequent cases add nothing to those reported by Meigs and Cass in 1937. The specific gravity of the fluid is that of a transudate; the presence of lymphocytes is noted, and the absence of tumor cells whenever looked for. Numerous attempts to obtain positive guinea-pig tests failed and in no instance was tuberculosis proved. Apparently the fluid is not in the nature of an inflammatory reaction. The blood studies were of no significance, and the elevation of the temperature was minimum. The serum protein in Case 10 was 7.1 mg. and in Case 15 it was 6.9 before operation and 7.3 at time of discharge. These figures are within normal limits.

*Preoperative Treatment.*—In many cases the chest and abdomen were tapped numerous times. Table II shows that abdominal paracenteses were performed about half as often as chest taps. It is to be noted that the chest

TABLE II  
SYNOPSIS OF 15 CASES WITH FIBROMA OF THE OVARY WHICH EVIDENCED SIGNS OR SYMPTOMS OF FLUID IN THE ABDOMEN AND CHEST

Case No. and Date	Author	Age	Status	Children	Chief Complaint	Tumor	Location of Effusion in Thorax	Thoracic centesis	Abdominal Paracentesis	Fluid at Operation
No. 1, March, 1879	Cullingworth <sup>1</sup>	36	M.	Yes	Metrorrhagia. Dyspnea. Colic	Bilateral	Left	0	0	Died without operation.
No. 2, April, 1901	M. G. H. <sup>10</sup>	42	S.	None	Pain in right chest	Ovary	Right	4	1	Considerable straw-colored ascitic fluid
No. 3, June, 1902	M. G. H. <sup>10</sup>	55	M.	Yes	Pleurisy	Right	Right	5	0	6 to 8 quarts ascitic fluid
No. 4, Oct., 1908	M. G. H. <sup>10</sup>	38	M.	Yes	Pain in shoulder, especially on left	Left	Right and left	7	4	Several quarts ascitic fluid
No. 5, July, 1917	Mayo <sup>4</sup>	36	M.	Yes	Bloating of abdomen. Cough. Loss of strength	Ovary	Left	1	0	Marked ascites
No. 6, Nov., 1920	Mayo <sup>4</sup>	53	M.	None	Bloating. Pain between scapulae	Right	Right	3	1	Several liters ascitic fluid
No. 7, March, 1926	Leo <sup>5</sup>	64	?	?	Dyspnea. Pain in chest	Left	Right	Repeated	0	Large amount of ascitic fluid
No. 8, April, 1928	de Rouville, <sup>12</sup> <i>et al.</i>	58	M.	Yes	Cough. Emaciation	Right	Left	1	9	1,000 cc. ascitic fluid
No. 9, April, 1932	Salmon <sup>14</sup>	52	M.	?	Abdominal mass, and cramps	Right	Right	3	0	500 cc. ascitic fluid
No. 10, Aug., 1934	M. G. H. <sup>10</sup>	52	S.	None	Dyspnea. Change in bowel habits	Left	Right	Repeated	1	Large amount yellow ascitic fluid
No. 11, July, 1936	Miller <sup>11</sup>	60	S.	None	Pressure. Weakness. Disability	Right	?	3	0	
No. 12, Aug., 1936	Weld <sup>18</sup>	55	?	?	Swelling of abdomen	Bilateral	Right	0	0	3,500 cc. ascitic fluid
No. 13, Sept., 1936	Weld <sup>18</sup>	50	M.	?	Enlargement of abdomen	Right	Right	0	0	Blood-tinged ascitic fluid
No. 14, Jan., 1937	Macomber <sup>7</sup>	33	S.	None	Tumor in abdomen.	Left	Right	1	1	Two quarts ascitic fluid
No. 15, Feb., 1937	Rhoads and Terrell <sup>12</sup>	57	M.	Yes	Dyspnea. Shortness of breath. Fatigue	Right	Right	5	0	750 cc. ascitic fluid

fluid reaccumulated with great rapidity, and relief was short in most instances.

*Operative Pathology.*—In all but two instances, a single fibroma of the ovary was found at operation. Since the first report, two patients have been found with bilateral fibromata. One would immediately suspect that these bilateral fibromata might be Krukenberg tumors of the ovary, *i.e.*, metastases in the ovary from a carcinoma of the stomach, except for the fact that one patient with bilateral tumors (Case 1) died, and at autopsy no mention was made of a gastric neoplasm. Krukenberg's original name for his tumor is "fibrosarcoma ovarii mucocellulare carcinomatodes"; therefore, it is reasonable to assume that they might easily be confused with true fibromata of the ovary. The other patient (Case 12) is known to have been well at least three months after her operation, and there has been no suspicion of gastric cancer. Abdominal fluid was found in every case, varying from small to very large amounts, and its color ranging from the usual straw color to serosanguineous. The tumors varied in size from 9 to well over 20 cm., and many of them were reported as being wedged in the pelvis.

There were no fatalities following the operation, and convalescence in nearly all instances was uncomplicated. In three patients fluid remained after operation but gradually receded and vanished. In only one patient (Case 6) was it necessary to do a chest tap after operation and this was done directly afterward. The patient who came to autopsy died suddenly while in the hospital and before any surgery was undertaken. She was in the hospital under observation for six months and finally died of severe dyspnea and a generalized collapse. It is most probable that, with our present knowledge, this patient would have survived.

*Histologic Pathology.*—All tumors were fibromata and were made up of interlacing bands of tough, white connective tissue with cystic areas. The cysts represent either areas of liquefaction following interference with the blood supply or follicle cysts that have grown large and have not been obliterated.

The fibrous connective tissue of the ovarian stroma, derived as it is from the primitive mesenchyme of the embryonic gonad, gives rise to the fibroma of the ovary. The fibromata under discussion are all simple tumors and no evidence of luteinization as in "xanthofibroma cellulare" has been demonstrated. It is probable that the abnormal bleeding occasionally occurring in this syndrome is due to changes of a proliferative type in the endometrium (Case 11) due to persistent follicle cysts rather than to lutein changes in the fibroma.

*End-Results.*—Except for one patient that died without being operated upon, the end-results are uniformly excellent, and in no instance has it been necessary for the patient to return for removal of fluid from the chest or abdomen. Now that 14 cases have been seen and followed after operation it is obvious that the treatment is satisfactory. If this entity is suspected in a patient, an effort should be made to prove it, and no patient should be refused exploratory operation in order to confirm the suspected diagnosis.

# FIBROMA OF OVARY

## A CHRONOLOGIC PRESENTATION OF ALL KNOWN CASE REPORTS (15) OF PATIENTS WITH FIBROMA OF THE OVARY COMPLICATED BY ASCITES AND HYDROTHORAX

**Case 1.**—Cullingworth<sup>1</sup>: A. K., age 35, a widow, was admitted to St. Mary's Hospital, Manchester, England, March 11, 1879. She stated that she had had a swelling in the right groin, which she first noticed after the birth of her fifth child five years before. This, however, had disappeared until December, 1878, when she again noticed it. At the time of admission, she was having a slight uterine hemorrhage, which had been present continuously for about three months, previous to which time she had menstruated regularly. The patient had a florid, healthy complexion, and had not suffered in her general health.

**Physical Examination.**—Two hard, solid, nodulated tumors were discovered in the pelvis. One occupied the right side and extended a little over to the left, lying in front of the uterus and immediately beneath the abdominal wall. It was freely movable within a limited area. The second tumor, larger than the first, lay behind the uterus, with its smaller end dipping down into Douglas's pouch which it completely filled, and its larger end rising up above the level of the fundus uteri. The tumors were not adherent to the surrounding parts, and there was no fluid noted, at this time, in the peritoneal cavity.

The uterine hemorrhage finally ceased about the middle of June, 1879, from which time the patient's health rapidly declined. She lost weight, and ascites supervened to such an extent that on being admitted as an inpatient, at the end of July, the girth of the abdomen at the umbilicus was 39½ inches (100.3 cm.). By August 12, 1879, it had increased to 42½ inches (108 cm.). She suffered also from pleurisy, first on the left side, where effusion took place, and subsequently over the greater part of the lower lobe of the right side, where loud friction sounds were audible to within a short time of her death. On September 10, 1879, the patient became suddenly worse, with symptoms of intense dyspnea and general collapse. She died on the following day.

**Autopsy.**—The left pleural cavity was found full of fluid, and the whole of the left lung entirely collapsed. On the right side, the lower lobe was firmly attached by recently formed adhesions to the diaphragm and chest wall, and the whole lung was congested and edematous.

There was a large quantity of fluid in the peritoneal cavity, and the peritoneum was thickened and opaque. The abdominal and pelvic viscera were healthy with the exception of the ovaries, each of which had become transformed into a solid tumor. The tumor of the right ovary lay in front of the uterus and right broad ligament, crossing over to the left of the median line. That of the left ovary was wedged firmly in the pelvis behind the uterus, some force being required to extract it. Neither tumor was adherent. Both were solid throughout, with the exception of a serous cyst, about one inch in diameter, which had formed in the substance of the growth on the right side, close beneath the capsule. The weights and measurement of the tumors were as follows:

	Weight	Length	Breadth	Thickness
Right:	9 oz. (255 Gm.)	5 ins. (12.7 cm.)	3¾ ins. (9.5 cm.)	2¼ ins. (5.7 cm.)
Left:	22 oz. (624 Gm.)	6 ins. (15.2 cm.)	5 ins. (12.7 cm.)	3 ins. (7.6 cm.)

The tumors were firm and nodulated, whitish-gray in color, with a smooth, glistening surface. It was evident that they had replaced the ovaries, no portion of the normal tissue of the ovary remaining. The cut surface was firm, dry, and homogeneous, of a whitish-yellow appearance, and presented numerous small openings, of the size of a pin's head, which were evidently small cysts, while the larger cyst, already described as existing at one part of the periphery, was seen to be filled with a glairy fluid. Numerous whitish bands, irregular in their course, passed in from the fibrous capsule and subdivided the tumor into lobes, which in many places had a concentric arrangement. The



portions of the tumor enclosed within these trabeculae were equally firm, presented a finely fibrous appearance, and were of a somewhat yellowish tinge.

The tumors were examined microscopically in the pathologic laboratory of Owens College, by Doctor Dreschfeld, who has kindly furnished the following report: "The microscopic structure is best seen in sections cut from a part of the tumor which had been placed at once in Müller's fluid and hardened. This section shows the tumor to consist of fine and coarse fibers, along with cellular elements, blood vessels, and small microscopic cysts. The blood vessels are numerous; the larger ones consist of fully-formed arteries and veins, with well-developed muscular walls; the smaller ones are found to be capillaries. The section also shows the existence of larger spaces, bounded by fine fibers which form a kind of lining membrane; they are not lined by endothelium, nor do they contain other than fluid contents; their well-formed fibrous boundary, however, shows them to be cysts and not mere breaks in the tissue. In a section prepared from a portion of the tumor hardened in spirits, the arrangement of the fibrous tissue is seen to better advantage, but the cellular elements and blood vessels appear much shrunken. The tumor is a fibroma. The cysts not being bounded by distinct epithelium are probably due to cystic degeneration of the primary tumor masses."

**Case 2.**—Massachusetts General Hospital: A female, age 42, single, entered the hospital, April 29, 1901, complaining of pain in the right chest of one week's duration. Pain had increased gradually and she had become short of breath. The catamenial history was negative until three years before, when she occasionally skipped a month. She had had no cough, dyspnea, or pain before the present illness.

*Physical Examination* showed a well-developed and well-nourished woman. The heart was negative. There was flatness over the right chest throughout, with diminished voice sound and fremitus. Respiration was also much diminished. The left chest was negative. The abdomen showed a large, hard mass extending up to the umbilicus. Several nodules, like small fibroids, could be felt over it.

On April 30, 1901, 80 ounces of clear fluid were aspirated from the right chest. This made the patient much more comfortable, but physical signs showed that there was still considerable fluid present. On May 3, 1901, 62 ounces were withdrawn, with much relief to the patient. (An inoculation from this chest fluid was made into a guinea-pig. The animal was found dead on May 21, 1901, and an autopsy was performed which showed no evidence of tuberculosis.) The patient made an uninterrupted convalescence and was discharged, much relieved, May 7, 1901.

On May 28, 1901, the patient was readmitted, complaining of cough with considerable yellowish sputum, without blood. For the past two weeks dyspnea had again steadily progressed, so that she was unable to lie on the left side, and could walk only with difficulty.

*Physical Examination* showed both lungs symmetrical with expansion of the left greater than the right. There was right chest flatness below the level of the spine of the scapular and second rib in front with dullness above these limits and tactile fremitus diminished above and absent below. The interspaces were slightly fuller over the right chest. Respiration was feeble and with diminished voice sounds. No râles were heard. Heart impulse was palpable in the fifth space in the anterior axillary line and dullness corresponded 15 cm. from the midsternum. The sounds were of good quality and there were no murmurs. Pulses were equal and synchronous, of low tension, small volume, and regular. The abdomen was convex both ways, abruptly prominent, and slightly fuller in the right lower quadrant. A hard mass could be felt rising from the pelvis to two fingers' breadth from the anterior superior spine on the right, thence to two fingers' breadth above the navel line and descending to the left; this mass was hard, nontender, nonfluctuant, and movable laterally and anteroposteriorly. The flanks were tympanitic. Vaginal examination showed that the introitus admitted two fingers with difficulty. The cervix was low, of normal size, conical, and pointed perpendicular to axis of the vagina. The same hard mass was felt in the left vault and the posterior

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culdesac. The body of the uterus could not be made out. Hemoglobin was 85 per cent and the white blood count 11,000. The urine was normal.

On May 29, the patient was uncomfortable from dyspnea all night. The right chest was tapped and 68½ ounces of clear, straw-colored fluid withdrawn, with a specific gravity of 1.016, slightly alkaline, and the albumin content was 3.2 per cent. A slight sediment contained mostly fibrin flakes with a few degenerated epithelial cells and leukocytes. No organisms were found.

On June 1, the right chest was again tapped and 58 ounces were withdrawn. The fluid was clear and straw-colored, with a specific gravity of 1.017, slightly alkaline, albumin 3 per cent.

On June 3, a surgical drainage of the thoracic effusion was done under cocaine anesthesia. An incision two inches long was made through the skin. A needle was introduced, followed by the escape of yellow fluid. A knife was passed in and an incision was made through the intercostal muscles and pleura between the seventh and eighth ribs. Two small tubes were introduced and about 48 ounces were evacuated.

On June 10, the patient spent a rather uncomfortable day. She was not draining so much; the abdominal growth seemed increasing in size, and there was a question of ascitic fluid. She was losing ground a little. On June 12, she had considerable pain and was draining profusely. Her abdomen was tapped and the fluid injected into a guinea-pig and found to be nontubercular. By July 2, the patient had lost strength. Her feet were swollen. The thoracic cavity was washed out every day and four ounces of foul pus withdrawn. There was considerable distention of the abdomen. The abdomen was tapped again on July 7, and over six pints of reddish fluid were withdrawn. On August 13, 1901, the patient was discharged much relieved.

On September 18, 1901, the patient reentered the hospital for operation for an abdominal tumor, considered to be a fibroid of the uterus. She had continued to improve and had gained eight pounds in the two weeks previous to admission.

Under ether anesthesia, an ovarian tumor was removed, September 20, 1901. A long, median suprapubic incision was made and the peritoneum opened with immediate escape of considerable straw-colored fluid. A large whitish mass presented. After some manipulation, with the breaking up of adhesions, a mass about the size of a child's head, very solid and whitish in color, was removed. The pedicle, including the tube, was tied off with heavy silk. On October 19, the patient was discharged well and in good condition.

The pathologic report showed the mass to be an irregularly rounded tumor, measuring 20 cm. in greatest diameter and weighing 2,440 Gm. On section, the surface was moist, with numerous small cystic cavities, and on one side a remnant of ovarian tissue could be identified. The outer surface was covered with thin, fibrous membrane in which were numerous thin-walled veins and some slight adhesions. The consistency was firm, almost cartilaginous, and at one place the surface was deeply fissured. The tube was normal. Microscopic examination showed the structure to be made up of interlacing masses of fibrous and muscular tissue, in places quite cellular, in others less so.

Throughout the growth were chink-like spaces which were evidently of vascular origin. A diagnosis of fibromyoma was made.

In December, 1902, the patient wrote that she was in excellent health and had been married the previous September.

**Case 3.**—Massachusetts General Hospital: A female, age 55, married, para 1, entered the hospital, June 9, 1902. Five months previously, she had had "pleurisy" with a slight cough and pain in the lower chest in front, not especially connected with respiration. She was confined to bed for three months, and had never been strong since. She was tapped five times in the right back and two to four quarts of fluid were removed. For the past two weeks, her abdomen, which had always been prominent, had increased rapidly in size. She was constipated but her bowels moved well with

cathartics. She had occasional vomiting without blood and considerable abdominal discomfort. Three years before, she had noticed a tumor moving from side to side in the lower abdomen; it moved spontaneously and felt "like a baby." She had no pain or discomfort from this mass.

*Physical Examination* showed a well-developed and poorly nourished woman, with fairly good color. She had a small, rapid pulse of low tension. The heart was negative. Respirations were slightly harsh all over, with an occasional r le, especially in the right base. There was dulness in the right axilla and right back below the angle of the scapula, with practically no respiration or voice sounds. Liver dulness began at the fifth rib in front. The abdomen was greatly distended, with shifting dulness in the flanks and tympany in the upper portion of the abdomen. There was a marked fluid wave. Nothing was palpable through the distended abdominal wall. There was slight dilatation of superficial veins. No edema of legs or face was noted. Pelvic examination showed a polyp, the size of an English walnut, presenting at the vulva with a narrow pedicle springing from the posterior wall of the interior of the cervix. Bimanual examination was unsatisfactory; the uterus appeared to be in good position and not enlarged. The culdesacs were full of fluid. There was slight tenderness in the left culdesac.

At operation, on June 10, under ether anesthesia, an incision was made in the median line below the umbilicus. The peritoneum was opened and six to eight quarts of yellow, clear fluid escaped. A mass in the right side was delivered into the wound and found to be an ovary the size of a coconut. A few adhesions were separated. The ovary and part of the tube were removed. Manual examination of other organs showed them to be apparently normal. On June 26, the patient was discharged well.

The pathologic report showed an irregular, lobulated mass covered for the most part by peritoneum. Weight 1 kg., 14 cm. in diameter. Adherent to one side was the fallopian tube, 6 cm. long, apparently normal. In one place the omentum, which contained many large vessels, was adherent. On section, there were masses of grayish tissue separated by bands of edematous connective tissue. A diagnosis of edematous fibromyoma was made. The patient died, October 25, 1913, 11 years postoperatively. The cause of death was given as senility and ventral hernia.

**Case 4.**—Massachusetts General Hospital: Female, age 38, married, para 2, entered the hospital, October 9, 1908, complaining of not having felt well for the past year. She had had some pain in her shoulders and back. Seven months previously she consulted a physician because of pain in the left side, which she described as sharp and knife-like and which prevented sleep. A left pleural effusion was found, the chest was tapped, and two quarts of fluid were withdrawn. She had been at rest, had been out of doors, and had had an extra diet with improvement, but the fluid returned very rapidly. About four weeks prior to her admission, she had noticed the abdomen increasing in size; this continued up to the time of admission. She had had some dyspnea on exertion for a good many years, but it had been worse since the fluid in the chest appeared and had become very greatly increased since the fluid in the abdomen had been noticed. She could not lie down flat but could walk up the stairs. For two days previous to her admission, her feet and legs had been swollen. A note from her local physician stated that her urine was normal. Three examinations of the sputum had been negative for tubercle bacilli.

Twelve months previously, a physician had found a uterine fibroid, and for two to three years previously she had felt something wrong in the region of the uterus. She had had no treatment. There had been no ascites.

*Physical Examination* showed a well-developed and well-nourished woman, with skin and mucous membranes of good color. She breathed easily in semirecumbent position or bed rest. No cervical, axillary, or inguinal nodes were palpable. The heart apex impulse was not seen or felt, but pulsation was felt best to the right of the sternum. The left border of dulness was not determined. The right border, in

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the fourth interspace, was 6.5 cm. to the right of the midsternum. Sounds were best heard to the right of the sternum. They were regular and of good quality. There were no murmurs. Pulses were synchronous, equal, regular, and of fair volume and tension. The left chest was flat throughout and breathing was distant and at the base behind close to the spine there was egophony. Tactile fremitus was absent. There was flatness below the fifth rib in the mammary line on the right. The line of flatness extended around the chest in a horizontal line to 2.5 cm. below the lower angle of the scapula in the back. Breathing throughout the right chest was normal. The abdomen was very prominent, the greatest girth being midway between the umbilicus and pubes, and measured 110 cm. The umbilicus was flush. The abdomen was tense but not rigid. No masses could be felt. No tenderness or shifting dullness was noted. A fluid wave was obtained. Liver dullness began at the fifth rib, the lower border not being determined. There was slight, soft edema of the feet and ankles.

On October 10, the patient's abdomen was tapped, 18 pints of clear yellow fluid being obtained, and the end of the trocar impinged against a solid tumor which somewhat interfered with the flow.

Report of the ascitic fluid showed nine quarts of clear straw-colored fluid, alkaline, specific gravity 1.018, albumin 2.4 per cent. A culture was taken. Smears showed a predominance of lymphocytes. Some of the fluid was injected into a guinea-pig; the animal was killed, November 14, 1908, and an autopsy showed no tuberculosis. On October 19, a skin tuberculin test was negative after 48 hours. The patient complained of abdominal pain radiating to the right chest, nausea, and frequent vomiting. She had no fever and there was no change in the physical signs.

The fluid in the abdomen increased while the fluid in the chest seemed to be less. On October 25, the patient's abdomen was again tapped, low down in the right flank, and 14 pints and nine ounces of a clear yellow fluid were obtained. Girth before tapping measured 100 cm. and after tapping 83 cm. Report of the ascitic fluid showed slightly cloudy, straw-colored fluid without clot, alkaline, specific gravity 1.017, albumin 2 per cent, endothelial cells 34 per cent, neutrophils 1 per cent. Bacteriologic report: One colony of *Staphylococcus albus* (considered a contamination).

On October 29, the left chest was tapped; it was thought best to remove only eight ounces because the fluid had been in the chest so long. Small amounts were to be taken out at intervals so as to encourage expansion of the lung. Report of the chest fluid: Pale yellow, straw-colored without clot, specific gravity 1.017, albumin 1.7 per cent. Smear of sediment showed a predominance of lymphocytes. Lymphocytes 55 per cent, endothelial cells 44 per cent, polymorphonuclear cells 1 per cent.

On November 3, eight ounces of fluid were removed from the left chest; there seemed to be no return of fluid after the last tapping. Breathing was easier. Skin tuberculin reaction, November 6, was strongly positive. On November 7, the left chest was again tapped and about eight ounces of fluid were removed. Immediately afterward, the abdomen was tapped in the right flank and 15 pints of fluid were removed. The girth of the abdomen after tapping was 88.5 cm.

On November 10, there was apparently less fluid in the chest. There was resonance to the third rib in front and midscapula behind. Breathing over this area was as good as on the unaffected side. There was a right border of cardiac dullness 4 cm. to the right of the median line.

The left chest was tapped, November 12, and eight to ten ounces of fluid were removed. Ascites increased and was associated with edema of legs. Chest signs remained unchanged. The patient was started on catharsis and diuresis, November 20, to see if the ascites would diminish. The girth of the abdomen was 108 cm. The abdomen was tapped, November 21, and 18 pints were obtained. On November 28, the girth of the abdomen had increased to 103.5 cm., and the patient had gained four pounds in weight in 24 hours. Vaginal examination at this time showed a mass filling the pelvis, crowding the cervix behind the pubes, continuous with the suprapubic tumor.



The tumor was very hard, irregular, nonelastic and in the median line. Operation was advised to relieve a suspected tuberculous condition of the peritoneum and for diagnosis of the uterine tumor.

On December 5, there was so much discomfort caused from the abdominal distention that it was tapped and 260 ounces of fluid were obtained, similar in character to that previously rumored. On December 8, the left chest was tapped and nearly two quarts of fluid were obtained. It was hoped that this would give the lung a better chance to expand.

Operation was performed, December 12. A two-inch median incision was made. The peritoneum was opened, and several quarts of a thin yellowish-brown fluid escaped. A solid ovarian tumor was then delivered with some difficulty, and was removed. Gauze was packed into the pelvis. The pedicle arising from the left broad ligament was tied off with silk and the ovary of that side removed. The abdomen was explored and nothing else abnormal was found.

The pathologic report showed a solid tumor occupying the region of the ovary, measuring about 20 cm. in diameter, flattened, and upon section having a white, fibrous surface with some areas slightly hemorrhagic in character. Microscopic examination showed a growth of fibrous tissue with rather numerous and large cells, traversed by vessels having a wall slightly differentiated from the surrounding tissue. A diagnosis of fibroma was made.

Following operation the patient continued to improve, but on December 31, she complained of sharp pain, on inspiration or coughing, in the right axilla. She was transferred to the Medical Service for further observation and treatment. Examination of the heart showed apex impulse not seen but felt faintly in fifth space  $8\frac{1}{2}$  cm. to the left of the midsternum 2 cm. inside the nipple line. Sounds were regular and of good quality. No murmurs were heard. The pulmonic second sound was greater than the aortic and not accentuated. The pulses were synchronous, equal, regular, and of fair volume and tension. The abdomen was slightly rounded, soft, and tympanitic throughout. There were no masses or tenderness. The liver was at the sixth rib to the costal border; the edge was not felt. The splenic edge was not felt. There was no edema.

On January 5, 1909, friction rub and pain in the side were still present, but aside from this the patient felt better and was up and about the ward all day. Potassium iodide was given, 10 gr. three times a day. She coughed a good deal for 24 hours.

On January 9, there was no fluid in the chest. There was a little dulness at the extreme left base posterior, but normal breathing was heard at the base. There was a coarse friction all over the left back below the scapula and in the axilla. The lungs were otherwise normal. She felt very well. There was no pain in her side. The patient was discharged, January 9, 1909.

On November 11, 1935, a communication from the patient stated that she was in good health and very active. Thirteen and one-half years previously ( $13\frac{1}{2}$  years postoperatively) she had had to undergo an operation for adhesions of intestines and removal of the appendix and several small tumors. A letter from the surgeon who performed the operation stated that the patient entered the hospital complaining of spotting of blood of two weeks' duration. Preoperative examination showed adhesions about the uterus and a soft, tender mass in the left adnexal region. A preliminary dilatation and curettage was performed, with negative findings. On opening the abdomen dense adhesions were encountered; many loops of the ileum were adhered to each other and to a mass in the pelvis. The uterus was completely buried in adhesions. The left ovary was buried in a mass of adhesions and consisted of numerous follicle cysts and fibrous tissues; it was dissected out, and together with the uterus (which was very slightly enlarged) was removed. Kidneys, liver, gallbladder, and upper abdomen were all palpated and were apparently negative. The specimens were examined grossly, but no sign of any malignancy was noted. The patient made an uneventful recovery.



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**Case 5.**—Mayo Clinic: Female, age 36, married, para 1, entered the hospital, July 31, 1917, complaining of a prolapsing uterus and "bloating" of the abdomen. After the birth of her child, three years prior to her admission to the clinic, the patient had been confined to bed for three weeks, menstruated considerably at the time, and for two or three weeks had felt a dragging sensation continually. After about one year, she had noticed a prolapse of the uterus, which gradually came down farther until it protruded four or five inches. At the same time, she had noticed bloating of the abdomen, which was diminished but not entirely reduced after urination, which phenomenon had been more evident during the last six months. Appetite poor. She was constipated at times and passed a yellow, mucus-like material with the fecal matter. There had been a foul discharge for five months. During the spring previous to her entry she had experienced sweats and chills, with some coughing and expectoration. She had steadily lost weight and strength, but there was no coughing or expectoration at the time of her admission.

The family history developed no evidence of cancer or tuberculosis. The patient's first menstrual period, at age 12, had been very painful; since then the periods had been regular. The patient had had a child at the age of 32, at which time the labor had been very difficult. Forceps had been used and there had resulted a bad tear.

*Physical Examination* revealed a blood pressure of 106/96. Examination of the chest revealed dulness and decrease in fremitus, more marked on the left side. The postcervical axillary nodes were slightly enlarged. The heart dropped a beat every six to 20 beats. The abdomen was distended with fluid, and there was tenderness and bulging over the flanks and a central tympany in a supine position, with a fluid wave. There were large masses attached to, and movable with, the uterus. The cervix was soft and dilated; menstrual discharge was present. A catheterized specimen of the urine revealed an occasional red blood cell. Hemoglobin 71 per cent; leukocytes 8,500. Roentgenologic examination of the chest revealed bilateral fluid extending as far as the seventh rib posteriorly.

In view of the latter finding, aspiration of the chest was carried out, August 4, following which the diagnosis of malignancy was raised. Roentgenologic examination after the aspiration showed some improvement in the chest condition.

On August 16, exploration was performed. A large tumor, the size of a child's head, was found, which had the clinical appearance of malignancy, but which the pathologist reported to be benign. There was marked ascites. The ovarian tumor was very adherent, was impacted in the pelvis, and was difficult to remove. The sigmoid flexure was short. The appendix was normal and was not disturbed. No gallstones could be felt. A subtotal abdominal hysterectomy with bilateral oophorectomy and salpingectomy was performed. The final pathologic report showed metritis, chronic salpingitis, and degenerating fibroma of the right ovary.

The patient's convalescence was uneventful and she left the hospital, August 30, 1917.

She returned to the Clinic again in August, 1921, at which time she stated that she had been well since her operation; her appetite was good, and she had gained 50 pounds in weight. She was again seen in September, 1921, at which time the general examination was essentially negative.

**Case 6.**—Mayo Clinic: Female, age 53, married, entered the hospital, November 26, 1920, complaining of bloating of the abdomen and some pain between the scapulae. Three years prior to the patient's admission she fell down 22 steps, after which the menses stopped completely and at that time she began to experience pain in the lower abdomen, which was more severe when she attempted to walk. Associated with this pain was considerable bloating, which was very severe at times. Steam-cabinet baths and abdominal massage gave considerable relief. Following an attack of pleurisy in 1915, there had been some substernal pain and moderate discomfort in the interscapular region. There was no evidence of an acid-fast infection, with the exception of

occasional night sweats. The gastro-intestinal history was essentially negative, and it was noted that there had been some dyspnea on exertion and occasional nocturia. Three years previous to the patient's entry, she had been hospitalized elsewhere and had had 40 ounces of fluid removed from the chest, and seven weeks later, 60 ounces of fluid were removed. The patient had been very dyspneic before her first hospitalization and was relieved only by tapping of the chest, with moderate abdominal ascites.

Her father had died of arteriosclerosis; in other respects the family history was essentially negative. She had been married 22 years but had never been pregnant. Menstrual periods had been normal until three years prior to her admission, at which time they had ceased completely. She had had diphtheria several years previously, influenza in 1898, and pleurisy in 1915.

*Physical Examination* revealed a blood pressure of 108/80. An area of dullness to flatness was noted in the lower right chest; no breath sounds were noted; there was an absence of tactile fremitus, whispered pectoriloquy was observed and increased vocal fremitus, amounting to bronchophony. The left border of the heart was just within the anterior axillary line, in all probability displaced and only slightly hypertrophic. The abdomen was dome-shaped, with signs of the presence of considerable fluid.

Uranalysis was essentially negative. Hemoglobin 73 per cent; red blood cells 4,600,000 and leukocytes 6,000. Roentgenologic examination of the chest showed fluid in the right chest up to the level of the second rib. A paracentesis was performed, November 30, 1920, and six and one-half liters of clear, straw-colored fluid were aspirated. On December 1, 1920, about 1,600 cc. of clear, straw-colored fluid were aspirated from the right chest; bacteriologic studies revealed no bacteria and no growth of organisms.

Abdominal exploration was carried out, December 9, 1920, through a midline incision. Several liters of straw-colored fluid were evacuated. A large, nodular, friable tumor (about the size of a large grapefruit) of the right ovary was found attached by a rather small pedicle, which was removed. The left ovary was about the size of a buckshot and was not disturbed. The uterus was normal in size and position. There was apparently no metastasis to the peritoneum or liver.

Pathologic examination showed an edematous, degenerating fibromyoma, with the remaining ovarian tissue flattened out over it.

Convalescence was essentially without incident, and she was discharged, January 14, 1921.

Five months later (June 21, 1921), the patient returned to the Clinic. She had gained 20 pounds in weight, and her general health was excellent. Abdominal and bimanual pelvic examination failed to reveal any trace of recurrence of the tumor.

**Case 7.**—Leo<sup>5</sup>: Female, age 64, was admitted to the hospital, March 25, 1926, complaining of dyspnea, cough, and pain in the right chest of several months' duration.

*Physical Examination* revealed a poor general condition, signs of a large pleural effusion in the right side of the chest, and a mass, the size of an adult's head, in the lower part of the abdomen.

Repeated chest taps were necessary to keep the patient comfortable, 1,000 cc. of fluid being removed every three or four days. This had the characteristics of a transudate and no definite diagnosis could be made by study of it. Tuberculin skin test was positive. Echinococcus skin test was negative. Shortly after admission, ascites developed and became quite marked. The patient ran a slightly elevated temperature.

Because of the downhill course of the patient and because of the apparent hopelessness of the situation, operation was performed, July 25, 1926. The abdomen was opened and a large amount of greenish-yellow fluid escaped. A large mass was found occupying the region of the left ovary. The uterus, the right ovary, and the other abdominal organs were normal, although no specific mention of the liver was made. The mass, which proved to be a benign tumor of the ovary, was removed.

After a stormy postoperative period, the patient finally recovered and was dis-

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charged on the twentieth day after operation. There had been no return of the fluid except for the withdrawal of 300 cc. of fluid from the right chest on the fifteenth day postoperative. No further chest taps were required.

On check-up, two months after discharge, the patient's general condition was excellent, and there was no evidence of fluid in either the chest or abdomen.

**Case 8.**—de Rouville,<sup>13</sup> *et al.*: Female, age 58, widow, para 4, was admitted to the hospital in April, 1928. The patient was very emaciated and had an enormous abdomen. One year before admission, she had "grippe" for three months, and this was accompanied by a productive cough. The "grippe" apparently over, the patient noticed an increasingly rapid enlargement of her abdomen, without pain. At the end of one month, she had an abdominal tap and 15 liters of hemorrhagic fluid were obtained. Seven other taps were performed within the next eight months. The fluid, always quite abundant, ceased to be hemorrhagic, and gradually became yellow. The general condition changed, almost bordering that of cachexia. Marked dyspnea was present.

*Physical Examination* showed a very distended abdomen. The puboxyphoid distance was 57 cm., and palpation gave a sense of resistance. Definite fluctuation was present. Percussion elicited the signs of free fluid. Vaginal examination revealed the signs of fluid in the culdesac. No tumor was felt. There was dulness over the left lung with a pleuritic rub over the apex. On exploratory puncture a little yellow fluid was aspirated. On the right side, there was nothing except râles at the base. There was a little edema of the legs.

An abdominal paracentesis was performed, May 1, 1928, and 18 liters of fluid were aspirated. After the fluid had been removed, four or five tumors could be felt under the abdominal wall—some above and some below the umbilicus; hard, tender, and freely movable, giving the impression of epiploic tumors. Vaginal examination confirmed the above findings.

Analysis of the ascitic fluid showed a slight lymphatic reaction. Analysis of the pleural fluid showed exactly the same findings. One week later eight liters of fluid were removed.

On May 10, 1928, an exploratory celiotomy was performed under local anesthesia. On opening the abdomen about one liter of yellow fluid escaped and a large multilobulated tumor was found. There were some adhesions of the mesentery which were easily broken up. The tumor was found to originate in the right ovary, and had a narrow pedicle which had been twisted many times. No other tumors were found.

The mass removed was as large as the head of a child and weighed 1,450 Gm. It consisted of a central cavity surrounded by a dense periphery. It proved to be a fibroma rich in fibroblasts; there were no mitotic figures. No characteristics of malignant disease were evident; only those of hyperplasia of the connective tissue.

Convalescence was uneventful, without recurrence of ascites or dyspnea, and the patient was discharged 20 days postoperative.

**Case 9.**—Salmon,<sup>14</sup> Hosp. No. 337,216: Female, age 52, was admitted to the hospital, April 7, 1932. For three months previous to admission she had been conscious of a mass in the lower abdomen which had increased steadily in size. Her chief complaint upon admission was irregular cramps in the lower abdomen of several days' duration, not accompanied by any gastro-intestinal symptoms. Temperature 100° F., pulse 74, respiration 22.

*Physical Examination.*—The patient was a fairly well-nourished female who did not appear acutely ill. Signs of fluid were found in the right chest. In the abdomen, a tense, tender, somewhat irregular mass could be felt arising from the pelvis and reaching to the umbilicus. Hemoglobin 78 per cent; white blood count, 9,000; polymorphonuclear neutrophils, 80 per cent; lymphocytes, 17 per cent; monocytes, 3 per cent. Sedimentation time 13 minutes. The urine examination and the Wassermann reaction were negative. The right chest was tapped, and 1,500 cc. of amber-colored fluid aspirated. Laboratory examina-

tion of the fluid revealed: Specific gravity 1.018; red blood cells, 1,800 per cubic millimeter; white blood cells, 350 per cubic millimeter; lymphocytes, 70 per cent; polymorphonuclear neutrophils, 30 per cent. No organisms were found on smear or culture. No tumor cells were found on centrifugalization. The fluid rapidly reaccumulated and the right chest was tapped again on two occasions, 1,500 and 2,000 cc. of straw-colored fluid being removed. Roentgenograms of the chest following the aspiration failed to reveal any abnormality in the lungs or chest wall to account for the effusion. Roentgenologic examination after the second aspiration disclosed a small amount of fluid also in the left chest.

Since no definite conclusions could be arrived at concerning the etiology of the effusion, it was felt that the nature of the pelvic tumor should be investigated. An exploratory celiotomy was, therefore, performed, and about 500 cc. of deep amber-colored fluid were found in the peritoneal cavity. A solid tumor of the right ovary, about the size of a large cantaloupe, was removed. The abdomen was thoroughly explored and no other abnormality was found. Convalescence was uneventful except that, on the eighth postoperative day, signs of fluid were detected in the right chest, and 500 cc. of serosanguineous fluid were aspirated. The pathologist reported the tumor as: "Edematous fibroma with necrosis."

It is now 24 months since the patient was discharged from the hospital. She has had no symptoms and has gained 40 pounds in weight. There are no signs of fluid in either the chest or abdomen. Roentgenologic examination of the chest reveals nothing abnormal.

**Case 10.**—Massachusetts General Hospital: Female, age 52, single, entered the hospital, August 4, 1934, with the complaint of changes in bowel habits and dyspnea on exertion of three months' duration. She had begun to have loose, watery stools containing mucus, three or four times a day. Shortly after the onset of the bowel discomfort she had noticed dyspnea on exertion of three months' duration. This had gradually become more marked, and on May 10, 1934, she was found to have fluid in the right chest. Considerable fluid was aspirated, with marked relief of the dyspnea. Subsequent taps at ten- to 14-day intervals were necessary to keep her comfortable. About two months prior to admission, she had noticed an increase in the size of her abdomen; frequent injections of salyrgan were administered, with some decrease in the size of the abdomen. There was marked decrease in her general strength and vitality. Her family history was negative.

*Physical Examination* revealed a patient quite ill, with signs of a large pleural effusion on the right side, and a large amount of fluid in the abdomen. Blood pressure 120/76. Heart normal. No edema of the extremities. No enlargement of any of the peripheral nodes. The liver edge was felt, in spite of the large amount of abdominal fluid, nearly down to the umbilicus. Pelvic examination revealed a hard, orange-sized mass in the left vault.

Urine examination was negative other than for the slightest possible trace of albumin and occasional white blood cells. Complete blood examination revealed a fairly marked secondary anemia: Hemoglobin 65 per cent. Red blood count 3,100,000; white blood count 12,000. The differential count was normal other than for 73 per cent polymorphonuclears. The red and white cells were normal except for achromia of the red cells. Repeated sputum examinations were negative. Repeated stool examinations were negative. Non-protein nitrogen 39 mg., serum protein 7.1 per cent, blood chlorides normal. Hinton test negative. Liver function test was normal. Roentgenologic examination of the chest revealed no abnormalities other than the large amount of fluid in the right chest. Gastro-intestinal series and barium enema were negative.

Two days after admission, 2,300 cc. of fluid were aspirated from the right chest with a replacement of 1,500 cc. of air. The fluid was a typical transudate. Examination failed to reveal the presence of any tumor cells or tubercle bacilli. Guinea-pig inoculation was likewise negative. Routine culture of fluid was negative. Abdominal tap revealed an identical fluid.

An exploratory celiotomy and left salpingo-oophorectomy were performed, August 18, 1934. The peritoneum was normal. The liver was markedly enlarged, the right lobe



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extending to the level of the umbilicus. It appeared, however, perfectly normal in appearance and to palpation. A large amount of yellowish fluid was evacuated. The spleen, stomach, intestinal tract and the kidneys were apparently normal. There was a small gallstone in the gallbladder, and the pancreas was normal. A large solid tumor, which filled the pelvis, and which included the left ovary, was removed. The uterus and right ovary were normal.

The pathologic report showed a very large, solid, firm mass 15x7.5x7 cm. Its cut surface was of a mottled yellow and white color with streaks of white crossing it in every direction. There were one or two areas which appeared finely granular. A diagnosis of fibroma was made.

The patient had a particularly smooth convalescence and was discharged three weeks after operation. Six months after discharge, there was no evidence of chest or abdominal fluid by examination and fluoroscopy. The liver was still enlarged, the lower border being felt about halfway to the umbilicus.

A letter, received in April, 1935, stated that a fluoroscopic examination showed a normal condition, and that her physician had said that, if anything, the right side and chest looked better than the left. She was heard from again in December, 1935, and stated that she was feeling perfectly well.

**Case 11.**—Miller<sup>11</sup>: L. K., female, age 60, single, had been ailing for several years. She had a large abdominal tumor which had caused a great deal of pressure, pain, weakness, and disability. Recently, she had had some fluid in her right chest and her local physician had tapped her two or three times.

*Physical Examination* showed a frail, thin woman. The heart action was regular but rapid. There was considerable dullness over the right chest but it became more resonant after the thoracentesis. Abdominal examination showed a large, hard tumor extending from the pelvis to the umbilicus.

At operation, July 16, 1936, under spinal anesthesia, a huge, solid tumor of the right ovary was found, which did not, however, look malignant. It was removed together with the uterus and the other ovary. The pathologic report showed the right ovary replaced by a large, solid mass, measuring 18x14x10.5 cm. Its surface was irregularly nodular, grayish-pink in color, and there were numerous subserous dilated veins. The tumor cut firmly and revealed a mottled, granular, reddish-gray surface with small, yellowish necrotic areas. In the central portion of the mass, there was a large multiloculated, smooth-walled cavity containing clear yellow fluid. A diagnosis was made of a fibroma of the ovary, follicular cysts of the ovary, endometrial polyp, leiomyoma, and cystic hyperplasia of the endometrium.

In June, 1938, the patient was free of any symptoms suggesting pleurisy with effusion or ascites.

**Case 12.**—Weld<sup>12</sup>: I. U., female, age 55, was admitted to the Gynecological Service of the Municipal Hospital, Hartford, August 21, 1936, complaining of swelling of the abdomen. About two months prior to admission, she had first noticed the swelling. She also complained of pain in both kidney regions and a low sacral backache. There was a history of chronic constipation.

The menopause had occurred at 35.

*Physical Examination* revealed a few coarse râles at the base of the right lung, with diminished breath sounds over the same area. The abdomen was shiny and taut; a fluid wave was elicited. A right inguinal hernia in addition to a herniorrhaphy scar was noted. Vaginal examination showed a large, hard, irregular mass filling the pelvis, reaching to two fingers' breadth below the umbilicus, immovable, with tenderness in the region of the sigmoid and rectum. The mass filled the posterior culdesac.

Roentgenologic examination of the chest the day after operation showed no evidence of tuberculosis, but there was increased density at the outer and lower portions of the right lower lobe, with irregularities of the diaphragm and partial obliteration of the costophrenic angle—all indicative of pleural exudate. Blood pressure 112/68. Blood



Wassermann and Kahn tests gave a two plus reaction. Blood nonprotein nitrogen 35.9 mg. per cent. The red blood cell count 4,030,000; with 85 per cent hemoglobin.

At operation, about 3,500 cc. of straw-colored fluid were removed from the peritoneal cavity by suction. A solid ovarian tumor 9 cm. in diameter, together with a multilocular cyst, was removed. The lower pelvis was then found to be filled with a second ovarian tumor, so situated that it predisposed to sigmoidal and rectal obstruction; it was delivered from the pelvis with some difficulty and was removed. Both tubes were then removed, and a supracervical hysterectomy performed. No lymph nodes were found in any part of the peritoneal cavity, nor was there any evidence of extension of the tumor masses to the bowel. There were no bowel adhesions. Each tumor apparently arose from an ovary. Grossly, the tumors appeared smooth and nodular; on section they were composed of dense, gray strands of fibrous tissue. Microscopic sections of the solid tumors showed typical fibromata, no anaplasia and no malignancy. In one or two areas, the pathologist reported the cells to be somewhat large and slightly hyperplastic. The cyst was lined by low epithelium, which, in focal areas, was thrown into a papillary arrangement. Here again, there was no evidence of malignancy.

The patient had an uneventful convalescence and was discharged on the seventeenth postoperative day. Roentgenologic examination of the chest, November 30, 1936, three months after operation, "showed no evidence of pleural effusion." An examination in October, 1938, showed the pelvis to be free from any masses, and there was no evidence of fluid in either cavity.

**Case 13.**—Weld<sup>18</sup>: E., female, age 50, married, was admitted to the Gynecological Service of the Hartford Hospital, September 15, 1936, complaining of progressive enlargement of the abdomen of six weeks' duration, and of difficulty in voiding for a relatively short time. During the previous six weeks, she had experienced lower abdominal pain, characterized as a heavy dragging sensation. Menopause occurred ten years prior to admission, and since then there had been no bleeding.

*Physical Examination* revealed a general appearance of illness; two lipomata on the back; signs of fluid in the right posterior chest; slight enlargement of the heart to the left; an elevated pulse rate; and a pelvic mass rising to the umbilicus, which gave the findings compatible with encapsulated fluid. Stereoscopic and lateral roentgenologic examination of the chest showed: "A moderately large amount of fluid in the right pleural cavity, extending into the interlobar fissures and apparently encapsulated in the axilla. The possibility of an underlying pathologic change in the right pulmonary field cannot be excluded without further examination made after a thoracentesis. The left lung is negative in appearance."

An operation was performed under spinal anesthesia three days after admission. The abdomen was opened through a lower midline incision, and was found to be filled with blood-tinged fluid. A solid, right ovarian tumor, with loops of bowel adherent to it, was visualized. The liver was smooth, and normal to palpation. There was no sign of malignant metastases. The uterus, left tube and ovary appeared normal. Only the tumor was removed.

*Pathologic Report.*—*Gross*: "Nodular mass, 15x12x11 cm., encapsulated. On section, it is composed of interlacing strands of rather soft fibrous tissue, through which there are extensive interstitial hemorrhages and dilated vessels. Over one surface is what appears to be a vessel containing blood clot. At one pole of the nodule there is a cyst three centimeters in diameter, having a ragged, seminecrotic lining. *Microscopic*: Multiple sections through the nodule show a rather cellular fibrous tissue proliferation. There are some mitotic figures; a few are not entirely regular. There are extensive areas of myxomatous degeneration, and large vascular spaces are scattered through the tissue, in some of which thrombi are present. Structure is fairly characteristic of a benign fibroma of ovarian stroma. *Diagnosis*: Fibroma of the ovary."

The patient was discharged on the nineteenth postoperative day, after an uneventful convalescence. Roentgenologic examination of the chest at that time showed less fluid

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than prior to operation. Roentgenograms of the chest seven months after operation showed no evidence of effusion.

**Case 14.**—Macomber<sup>7</sup>: Female, age 32, single, entered the hospital, January 7, 1937. Three years previously, her abdomen began to enlarge and this continued steadily without discomfort or inconvenience until recent months. Being a Christian Scientist, she had not consulted a physician until a short time before admission. About one month previously, the swelling had reached such proportions as to interfere with walking, and she began to have marked dyspnea. This came on quite suddenly and was very severe for one week but then continued with less severity. There was no chest pain other than a feeling of soreness retrosternally. Four months, and again two months, before entry she noticed a small hole just below the umbilicus which discharged fluid for several days. No bowel or urinary symptoms. Catamenia always somewhat irregular but she continued to have menstrual periods during the present illness, the last few more profuse. She has never vomited. On a few occasions she had a sudden breath-taking pain when lying on her left side. No swelling of ankles at any time. There was no cough, sputum, or hemoptysis at any time. Nine years previously, she had several episodes of severe pain in her left lower quadrant. She believes she had lost a good deal of subcutaneous fat but had gained ten pounds, which she attributed to the abdominal fluid.

*Physical Examination* showed a somewhat thin woman. Heart apparently normal. The patient was obviously cachectic, probably somewhat anemic. The right chest contained fluid. The whole abdomen was tremendously enlarged, and was filled with fluid; it also showed some evidence of containing irregular masses. Rectal examination was practically negative. Roentgenologic examination showed fluid in the chest and abdomen, with displacement of the bowel and fixation of the left side of the diaphragm, probably due to tumors; consistent with adenocarcinoma of the ovary.

On January 9, 1937, the patient's abdomen was tapped, and 292 ounces of fluid obtained. On January 11, 1937, the chest was tapped, and 32 ounces of fluid aspirated. The abdominal fluid showed a specific gravity of 1.016. Differential count showed lymphocytes 19 per cent, polynuclears 2 per cent, monocytes 3 per cent, red blood cell count 18 per cent. The chest fluid showed 1,520 cells per 1/16 square mm. Differential could not be identified by smear. Very slight sediment was found and the fluid was straw-colored. No tumor cells could be identified. A day or two after this, she developed "acute bronchitis" and she was discharged in order to recuperate before operation was undertaken. Her abdomen continued to fill up, and her chest was again tapped at home, February 7, 1937.

The patient was readmitted to the hospital, February 14, 1937, for operation. Under spinal anesthesia, February 15, 1937, a left oophorectomy was performed. The abdomen was opened through a 12-inch median incision. An umbilical hernia was dissected out. No adhesions were found. About two quarts of clear fluid evacuated. The tumor proved to be a fibroma of the left ovary, the size of a rather large full term uterus, filling the entire abdomen, showing a certain amount of cystic degeneration, and weighing about 25 pounds. The tumor was removed. Section proved it to contain a cavity containing about two quarts of fluid. Some of the fluid was lost in removal. No obvious evidence of malignancy was seen. The uterus seemed normal; there were no peritoneal implantations. A normal tube and ovary and small uterus were left.

No acid-fast bacilli found in the sputum, which was examined, February 20, 1937. Roentgenograms of the chest, February 27, showed that the fluid in the left side of the chest had completely disappeared. There was a haziness at the left base, apparently due to thickening of the pleura. The patient had an uneventful convalescence and was discharged, March 6, 1937.

The pathologic report showed a rounded, smooth, grayish, firm, previously opened mass, measuring 25x22x18 cm. Through the grayish capsule could be seen several darkish, cystic areas, which on section were previously opened cysts containing clotted blood. The lining membrane was grayish, smooth, and glistening. The central portion

was made up of multilocular cysts, the largest measuring 15x9x7 cm. The grayish, firm tissue presented a smooth, glistening, firm surface. A diagnosis of a degenerated fibroma was made.

On June 28, 1937, the patient was seen and the scar was solid. Air passed well to bases of lungs. She had gained 12 pounds since April, 1937.

**Case 15.**—Rhoads and Terrell<sup>12</sup>: E. P., female, age 57, widow, para 3, was admitted to the hospital of the University of Pennsylvania, in the service of Dr. Alfred Stengel, February 1, 1937, complaining of shortness of breath, fatigue and the loss of 18 per cent of her body weight.

Her symptoms were first noticed in 1933, and had grown gradually worse. Dyspnea, at this time, developed when she ascended one flight of stairs, or merely with excitement. When she became dyspneic, a dry cough developed, but she had never had hemoptysis or pain in the chest. Palpitation had been noted during attacks of dyspnea and fatigue. She had never observed any peripheral edema. There were no digestive symptoms except for moderate anorexia and belching. She had never had any abdominal pain nor had she ever complained of abdominal fullness or distention.

The menopause occurred at age 53, four years before the present admission. The menses had begun at age 15, and had always been regular. There had been no post-menopausal bleeding or discharge. For many years, the patient had been under the care of a physician, who had noted a large pelvic tumor in the median line, at least eight years previous to her admission, which had not grown appreciably during the interval.

**Physical Examination.**—The patient was thin and rather cachectic looking and was prematurely aged. Examination of the chest revealed signs of a massive pleural effusion on the right side. The trachea was deviated somewhat to the left and the apex of the heart was displaced toward the left. There were no other abnormal physical signs in the left side of the chest. These observations were confirmed roentgenologically. Abdominal examination indicated the presence of a small amount of ascites. In the right upper quadrant, the liver was palpable three fingers' breadth below the costal margin. A large, round, firm tumor extended from the pelvis to a point midway between the symphysis pubis and the umbilicus. On pelvic examination this appeared to be attached to the cervix; it was firm, freely movable with the uterus and not tender. The pelvic mass prevented satisfactory palpation of the adnexa. There were no nodules felt in the culdesac. Temperature 98° F., pulse 90, respiration 20, blood pressure 130/85. Because of the ascites and hydrothorax, a tentative diagnosis of uterine sarcoma with metastases was made.

Thoracentesis was performed five times. The fluid removed from the right pleural cavity amounted to: February 2, 1,900 cc.; February 5, 1,000 cc.; February 10, 3,000 cc.; February 19, 2,000 cc.; and March 3, 1,000 cc. One and one-half liters of air were injected in an attempt to obtain better roentgenographic visualization of the pleura and right lung field. Within nine days, roentgenologic examination of the chest showed a reaccumulation of a large amount of fluid. So rapid was this reaccumulation, that there was a large mediastinal herniation, containing both air and fluid, which extended to the midportion of the left lung field. This necessitated removal of 2,000 cc. of fluid, for relief of the dyspnea.

**Laboratory Data:** Red blood cells 5,500,000; white blood cells 18,200; hemoglobin 98 per cent. Polymorphonuclear cells 75 per cent, lymphocytes 22 per cent, monocytes 2 per cent, eosinophils 1 per cent. Subsequent blood counts never disclosed a leukocytosis. Repeated uranalyses showed a specific gravity varying from 1.012 to 1.027, an occasional trace of albumin and a moderate number of white blood cells. The Kolmer and Kahn tests were negative for syphilis. The urea nitrogen content of the blood 15 mg. per 100 cc. Serum protein determination was 6.9 Gm. per 100 cc. Sedimentation rate 22 mm. in 60 minutes.

The pleural fluid obtained, February 2, showed a specific gravity of 1.021. It contained 450 cells per cubic millimeter (96 per cent mononuclear and 4 per cent poly-

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morphonuclear) and 1.75 Gm. of protein per liter. February 5, fluid with similar specific gravity showed, on long centrifugation, only an occasional normal red blood cell and a few lymphocytes and polymorphonuclear cells. No mitotic cells were found. None of the cells appeared malignant. February 19, the specific gravity was 1.014, the protein was 1 Gm. per liter and the cell count was 514 cells, with 86 per cent mononuclear and 14 per cent polymorphonuclear cells. Cultures of the fluid were repeatedly negative; guinea-pig inoculation was made on two occasions, but tuberculosis did not develop in the animals.

TABLE III

Ages.....	33-64
Status:	
Single.....	4
Married.....	9
Unknown.....	2
Fertility:	
Children.....	6
No children.....	5
Unknown.....	4
Location of tumor:	
Left ovary.....	4
Right ovary.....	6
Both ovaries.....	2
Unknown.....	3
Taps:	
Abdominal.....	6
Chest.....	12
Location of effusion in thorax:	
Left side.....	3
Right side.....	10
Both sides.....	1
Unknown.....	1

Because numerous roentgenologic examinations following injections of air did not show the expected pleural or pulmonary metastatic lesion, thoracoscopy was considered. It did not offer the patient much prospect of benefit, however. At this time the gynecologic consultant, Dr. Franklin Payne, suggested that the pelvic tumor might be an ovarian fibroma, and be presenting the syndrome described by Meigs and Cass.<sup>10</sup>

Accordingly, March 4, 1937, an exploratory celiotomy was performed by Dr. I. S. Ravdin. A moderate amount, probably in excess of 750 cc. of ascitic fluid, was evacuated. The pelvic mass proved to be a tumor of the right ovary, measuring 14x10.5x10 cm. It was readily removed. Exploration of the remainder of the peritoneal cavity showed no abnormalities. Convalescence from operation was smooth and uneventful. The last pleural aspiration was performed on the day before operation, when 1,000 cc. of fluid were removed.

Roentgenograms of the chest, taken on the sixth and fifteenth postoperative days, showed progressive diminution in the pleural effusion and reexpansion of the right lung. The patient did not require thoracentesis following the operation. At the time of discharge, March 23, 1937, the blood count was entirely normal, the serum protein was 7.3 Gm. per 100 cc., and the patient was subjectively cured and objectively improved.

Follow-up examination, April 22, 1937, seven weeks following operation: The patient was feeling very well; an excellent appetite had replaced the anorexia; she had no

symptoms of breathlessness, cough or fatigue; and she had gained weight. Physical examination was negative except for the signs of a very small amount of fluid or thickened pleura at the right base. Roentgenologic examination at this time showed great improvement in the appearance of the right lung field. The entire right lung had reexpanded, and there was only a small amount of fluid above the dome of the diaphragm. The pleura appeared somewhat thickened.

TABLE IV  
FINDINGS AT OPERATION

Case No.	Fluid	Amount	Adhesions	Size	Position
1	?	Large quantity (autopsy)	No	12 cm. 15 cm.	Both ovaries
2	Straw	Considerable	Yes	20 cm.	Ovary
3	Clear	6 to 8 quarts	Yes	14 cm.	Right ovary
4	Yellow-brown	Several quarts	Yes	20 cm.	Left ovary
5	Ascitic	Marked	Extreme	Child's head	Ovary
6	Straw	Several liters	Doubtful	Grapefruit	Right ovary
7	Green-yellow	Large amount	Doubtful	Large	Left ovary
8	Yellow	1 liter	Yes	Child's head	Right ovary
9	Deep amber	500 cc.	?	Large cantaloupe	Right ovary
10	Yellowish	Large amount	?	15 cm.	Left ovary
11	?	? (fluid in abdomen)	?	18 cm.	Right ovary
12	Straw	3,500	No	9 cm.	Both ovaries
13	Blood-tinged	?	Yes	15 cm.	Right ovary
14	Clear	2 quarts	No	25 cm.	Left ovary
15	Ascitic	750 cc.	?	14 cm.	Right ovary

TABLE V

Case No.	Entered Hospital	Operation	Follow-Up
1	March 11, 1879	Died without operation	September 10, 1879 (died)
2	April 29, 1901	September 20, 1901	December, 1902
3	June 9, 1902	June 10, 1902	October 25, 1913 (died)
4	October 9, 1908	December 12, 1908	November 11, 1935
5	July 31, 1917	August 16, 1917	September, 1921
6	November 26, 1920	December 9, 1920	June 21, 1921
7	March 25, 1926	July 25, 1926	October, 1926
8	April, 1928	May 1, 1928	?
9	April 7, 1932	?	April, 1934
10	August 4, 1934	August 18, 1934	December, 1935
11	July 16, 1936	July 16, 1936	June, 1938
12	August 21, 1936	August, 1936	November 30, 1936
13	September 15, 1936	September 18, 1936	April, 1937
14	January 7, 1937	February 15, 1937	June 28, 1937
15	February 1, 1937	March 4, 1937	April 22, 1937

*Pathologic Examination.*—The tumor weighed 8.0 Gm. It was rounded and smooth. The surface was traversed by a few moderately large vessels. The consistency was firm, approximately that of a squash ball. The tumor appeared to be a diffuse enlargement of the ovary. On section, it showed whorls of fibrous tissue such as those often seen in uterine fibromyomata. No cystic areas were found. Sections were cut at right angles to the surface and stained with hematoxylin and eosin. The tumor appeared to be composed of fibrous tissue with numerous fibroblasts. This was interspersed, in every



low power field, with eosin-staining areas having the appearance of smooth muscle. The Masson stain, which colors fibroblasts purple and muscle cells green, definitely established the presence of both elements. The pathologic diagnosis was stromatogenous fibromyoma of the ovary.

DISCUSSION.—The problem of why fibromata of the ovary may be accompanied by fluid in the chest and abdomen is so far unsolved. Various suggestions have been made and valid objections have been brought against each. The most obvious suggestions are anatomic or changes in the body chemistry. The work of St. Karady, Browne and Selye<sup>17</sup> on the "alarm reaction" must be discussed. Let us consider the anatomic features first: In the two-month-old human embryo the abdominal and pleural cavities connect. Later, this connection is broken by the presence of the diaphragm. Malformations of this broad muscle do occur and there are diaphragmatic herniae without sacs, where free communication exists between the abdomen and chest. In the event of a defect of this type in a woman with a fibroma of the ovary and with fluid in the abdomen, fluid would also be expected to be found in the chest. But that this rare anatomic anomaly could explain all cases in this rare syndrome does not seem probable. Drainage of either cavity in such an anatomic set-up should drain the other cavity, and this does not occur. Large diaphragmatic herniae are not uncommon and a sac is usually present. It is not possible to see how such a lesion could account for chest fluid except that abdominal fluid might fill the sac. An abdominal paracentesis should drain the chest and yet it does not. Small openings in the diaphragm can be conceived of, but their rarity and the unusualness of this condition rule out the possibility. It is difficult to believe any anatomic lesion is responsible for this syndrome.

An explanation on a chemical basis (protein deficiency) is a distinct possibility, but in only two cases have determinations of the serum protein been made. In both cases, the serum protein was found to be within normal limits—7.1 mg. in Case 10, and 6.9 mg. before operation in Case 15 and 7.3 after operation. In neither case was the serum albumin-serum globulin ratio known. It is interesting to note that three patients had very moderate peripheral edema of the legs. It is difficult to believe that protein deficiency can account for massive effusion and ascites without more evidence of peripheral edema. One can conceive of changes in the serum protein after multiple withdrawals of fluid, but this does not explain the original cause of the fluid. A circulatory phenomenon affecting capillaries and lymph vessels, with stasis sufficient to produce pleural effusion and ascites, should be accompanied by peripheral edema. Shock, with changes in blood volume and peripheral vasoconstriction and tissue edema, does not offer an explanation for the two large collections of fluid.

The "alarm reaction" of Selye with accumulations of pleural and peritoneal fluid is a constant finding when animals are exposed to damaging agents. Doctor Selye writes that "this was particularly obvious in cases in which irritating substances had been introduced into the peritoneal cavity." He considers it possible that "the fibroma might have acted as an irritating agent and that the

accumulation of pleural fluid was a direct result of the ovarian tumor." In this experimental work in animals (rats) it has been shown that repeated minor traumata cause a resistance to be built up and the appearances and functions of the organs return practically to normal. After a period of one to three months, with continued injury, the animals lose their resistance and succumb with symptoms similar to histamine toxicosis or surgical or anaphylactic shock plus accumulations of a peritoneal and pleural transudate. It is possible then to think of the fibroma as an irritating and shocking agent. At some time in the patient's life a general adaptation to continued injury is brought about, but later, due to its continued presence, a chronic form of "general alarm" phenomena sets in.

Selye's "alarm reaction" appears to the author to be the most satisfactory explanation so far for the presence of the fluid, but it must be admitted that this is not perfect.

Other pelvic lesions of a benign type may cause this syndrome; for instance, U. J. Salmon,<sup>14</sup> in 1934, reported a patient with a large fibroid uterus with some intraligamentous development who had sanguineous fluid in the right chest and abdomen. Seventeen months after operation, careful study revealed no evidence of residual disease or fluid. In the discussion of Meigs and Cass's<sup>10</sup> paper in 1937, W. T. Dannreuther presented a patient with a benign ovarian cyst who had fluid in her chest and later, after the operation, the fluid completely disappeared. It is possible, therefore, that there are other benign tumorous conditions in the pelvis besides fibroma of the ovary which may be accompanied by ascites and hydrothorax.

#### CONCLUSIONS

(1) Fifteen cases of fibroma of the ovary with ascites and hydrothorax are presented.

(2) In spite of increasing interest in the subject, no adequate explanation of either the ascites or hydrothorax has been suggested.

(3) The "alarm reaction" of Selye offers a better explanation than anatomic or chemical ones.

(4) The importance of this syndrome to patients suspected of some fatal disease is obvious. More search should be made in patients considered to have metastatic cancer for this benign entity.

(5) The possibility of this syndrome should always be in the mind of the internist and surgeon.

Thanks are due to many who have willingly helped and discussed this problem with me. I especially wish to acknowledge my indebtedness to Drs. Edward Churchill, Leland S. McKittrick, Isidor Ravdin, U. J. Salmon, Donald Macomber, Richard H. Miller, Peter Gruenwald, Cecil Drinker and J. S. L. Browne.

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DISCUSSION.—DR. WILLIAM F. MACFEE (New York): In connection with Doctor Meigs' paper, I should like to mention a case that came to my attention last November. The patient, female, age 54, gave a history of progressive enlargement of the abdomen for a period of one year. During that time she noticed a loss of weight from other parts of her body, progressive emaciation, loss of strength, and for about one month she had had very distressing dyspnea which practically disabled her.

Upon admission to the hospital, the positive findings were an enormous enlargement of the abdomen with marked emaciation elsewhere. On percussion, the abdomen was entirely flat throughout. Tympany was absent even over the stomach, and there was all the evidence of fluid in the abdomen.

In addition, the right chest was completely flat to percussion and the breath sounds were absent. The presence of fluid in the chest was confirmed roentgenologically. The chest was aspirated and 1,500 cc. of a greenish-brown fluid were removed. Tubercle bacilli could not be demonstrated and nothing except a few lymphocytes and some desquamated pleuritic cells were found.

The patient appeared to be in the final stages of malignant disease of the ovary. With the idea of palliation rather than cure, operation was advised in the hope that removal of the large cyst might afford some relief from her distress.

At operation, a very large cyst was found lying rather free in the abdomen, surrounded by a thin film of free abdominal fluid. The cyst was removed without difficulty, and the patient had a relatively uneventful convalescence. Ten days after operation, however, it was necessary to aspirate the chest once more because of reaccumulation of the fluid. Her course after the second

aspiration was free of further complications. She made a good recovery and is well to-day.

Pathologic examination of the tumor showed it to be a cystic adenoma, multilocular in type, with no evidence whatever of malignancy.

I think the profession owes a great deal to Doctor Meigs for calling attention to this condition in which there is fluid in the chest associated with a benign tumor of the ovary. Recognition of this possibility may very well lead to a more careful investigation of cases of this kind, and to the saving of a certain number of patients who otherwise might needlessly die.

DR. JAMES C. MASSON (Rochester, Minn.): I think the paper Doctor Meigs has presented is a most interesting one, and the syndrome he has described is something we should all look for. From January 1, 1910, to December 31, 1938, there were 428 cases of ovarian fibroids listed in the records of the Mayo Clinic. In many of the earlier cases no roentgenograms of the thorax were made, and it is impossible for me to speak definitely about small collections of fluid in the thorax, because such a condition was mentioned in only two instances.

This syndrome is an important point to keep in mind when patients having ascites and pleural effusion are seen. There is no doubt that in the past all such patients were considered to have a malignant process, and most of them refused surgical treatment. No doubt the patient in an occasional case in which the collection of fluid is due to this benign condition is refused surgical treatment at a time when a relatively safe operation would be possible.

Ninety-one patients for whom a postoperative diagnosis of fibroma of the ovary was made have been encountered at the Mayo Clinic during the last four years. Of the fibromata present in these 91 patients, 23 were 5 cm. or more in diameter, and ten were bilateral. Routine roentgenograms of the thorax were made in practically all of these cases before operation, and in no instance was the presence of fluid noted, but from a small amount to several hundred cubic centimeters of fluid were noted in the abdomen in a great many cases. Just why a few of these tumors cause fluid to accumulate in the thorax as well as in the abdomen (and a great majority do not) is hard to explain.

It happened that since I was first asked to discuss this paper I have operated upon two cases of fibroma of the ovary. Both of these tumors were about the same size (15x12x10 cm.). Very marked fatty degeneration was present in the first one, which originally was a typical fibroma. A simple cyst was also present in the same ovary. It was hard to recognize any normal ovarian tissue. Several hundred cubic centimeters of fluid were present in the abdomen of this patient, but there was no indication of any change in the thorax.

The patient's history in the case involving the second fibroma was practically the same as that for the first patient, but I suspected the possibility of the presence of malignancy in this woman, and I therefore did a total hysterectomy, removing the left ovary as well, and in it was found another small fibroma.

I think that Doctor Meigs has drawn attention to a very important condition, and I am satisfied that if all surgeons are on the alert for this syndrome and advise operation in cases in which there is not a definite proof of metastasis in the thorax, more of these cases will be discovered.

DR. JOE VINCENT MEIGS (closing): I hoped somebody from the Presbyterian Hospital would say something, because I heard last week, when in New York, that they had had a patient there who had died, in whom they found fluid in both the abdomen and chest. At autopsy, a fibroma of the ovary was found. I feel there must be many more cases, and I think in the future they probably will be reported.

## THE EFFECT OF DISTENTION OF THE COLON AND STIMULATION OF ITS NERVE SUPPLY ON THE FLOW OF BILE FROM THE LIVER\*

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STASIS OF BILE is considered an important factor in the etiology and symptomatology of cholecystic disease or malfunction. When present, certain chemical changes in the gallbladder bile take place<sup>1</sup> which may influence the formation of calculi. Although it is well known that physiologic or pathologic disturbances of the biliary system may inhibit the flow of bile,<sup>2</sup> there is also evidence to show that changes elsewhere in the body may cause a similar effect.

The gallbladder of pregnant women have been found to be more distended<sup>3</sup> and their emptying times more prolonged than normal.<sup>4</sup> This delay in evacuation may be due (a) to the action of the sex hormones of pregnancy; (b) to a reflex inhibition of bile formation; (c) to reflex inhibition of the gallbladder; (d) to a reflex contraction of the sphincter of Oddi or the choledochoduodenal mechanism; and (e) to metabolic changes in the chemistry of bile. Biliary stasis during the latter part of pregnancy is associated with a low bile salt and high cholesterol content in the gallbladder bile, thereby favoring the precipitation of cholesterol out of solution.<sup>5</sup> Its presence may partially explain the symptomatology referable to the organ during pregnancy and the high incidence<sup>6</sup> of cholecystic disease afterwards.

The occurrence of constipation during and after pregnancy is well known. Blalock<sup>7</sup> has reported it as a symptom of gallbladder disease in 62 per cent of 735 patients in whom gallbladder disease was proven at operation. The incidence of cholecystopathy has been found to be doubled in patients with diverticulosis of the colon<sup>8</sup> and in patients with peptic ulcer or recurring appendicitis.<sup>9</sup> Boyden and Birch<sup>10</sup> have shown that stimulation of the duodenum, jejunum and cecum in animals inhibits evacuation of the gallbladder. Many observers<sup>11</sup> have reported a high incidence of irritable colon in patients with organic cholecystitis, biliary dyskinesia or abnormal visualization by cholecystography. Lahey and Jordan<sup>12</sup> have observed improvement of the gallbladder shadow in 44 of 65 patients, who had absent or faint roentgenologic visualization after their irritable colon was treated a short period. Kunath,<sup>13</sup> in discussing the symptomatology of the stoneless gallbladder, suggests that a spastic biliary tract might accompany a spastic intestinal tract. Proper management of constipation or irritable colon, when present, often ameliorates the symptoms referable to the biliary tract.

\* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.



The foregoing evidence indicates the possible existence of a causal relationship between abnormal function of the colon and cholecystopathy. Disturbances of the colon might predispose to cholecystopathy (a) by reflexly inhibiting the flow of bile from the liver; (b) by reflexly causing hypertonicity of the sphincter of Oddi and the duodenum; and (c) by reflexly inhibiting the evacuation of the gallbladder. This investigation was undertaken to determine whether stimuli from the colon could reflexly inhibit the flow of bile from the liver.

*Methods.*—The experiments were all of the acute type, performed upon dogs fasted for 18 hours and anesthetized with sodium pentobarbital. The trachea was cannulated and the carotid blood pressure recorded. The cystic duct was ligated near its entrance into the common bile duct and the latter was cannulated close to the duodenum. The drops of bile were recorded on a revolving kymograph by an electrical recorder. It was usually necessary to wait 15 to 25 minutes before a regular control flow was obtained. A ligature was placed about the sigmoid colon just above the pelvic floor and another around the terminal ileum. A large cannula, through which the colon was slowly distended with tap water at 40°C., was inserted into the "appendix" and held in place by means of a purse-string suture. The amount of fluid injected depended upon the size of the dog and varied from 200 to 500 cc. The colon was never distended beyond the stage of compressibility and was permitted to remain distended for a five- to ten-minute period.

The only possible source of technical error in these experiments was the effect of kinking of the common duct at the site of entrance of the glass cannula. The distended colon occasionally angulated the small rubber tube attached to the cannula so as to obstruct the flow of bile. This could always be readily recognized by the presence of an increased flow above the control rate, during or immediately following deflation of the colon. At times it was necessary to gently retract the colon manually to the left side of the abdomen to obviate this possibility. Although this source of error was not as likely to be present while the nerves were being stimulated, it had to be constantly kept in mind.

The central cut end of the nerves was stimulated for a five-minute period with a shielded electrode which received its current from an inductorium, the source of electricity being two dry cell batteries. The secondary coil was set at from 3 to 6.5 cm., depending upon the degree of stimulation to the animal and the degree of rise in blood pressure.

*Results.*—*Distention of the Colon* (Table I).—Distention of the entire colon was associated with an inhibition of bile flow in 12 of 14 dogs (Graph 1). The diminished flow ranged from 18 to 80 per cent below the control level, or an average of —48.5 per cent, and was coexistent with a rise in blood pressure from 5 to 30 Mm. Hg. Although two dogs showed a normal blood pressure level, distention of the colon produced no change in bile flow in one (Table I, No. 16) and only a diminution of 8 per cent in the other (Table I, No. 10). These results are not significant and are recorded as not

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effective. Distention of the distal half of the colon in three dogs and the proximal half in two produced no change in the former group and only a slight inhibition in the latter. This suggests that the proximal is more sensitive than the distal colon.

TABLE I  
RESULTS OF EFFECT OF DISTENTION OF THE COLON ON RATE OF BILE FLOW  
BEFORE AND AFTER SECTION OF HEPATIC NERVES

Dog No.	Distention of Colon			Section Hepatic Nerves			Distention of Colon After Section Hepatic Nerves		
	Bile Flow —Cc. Per Hour*	During† Disten- tion— Cc. Per Hour	Per Cent Change	Con- trol —Cc. Per Hour	After‡ Sec- tion —Cc. Per Hour	Per Cent Change	Con- trol —Cc. Per Hour	During Disten- tion— Cc. Per Hour	Per Cent Change
2	5.4	3.6	-33%						
3	7.8	5.1	-35%						
4	1.5	0.3	-80%						
5	6.3	2.7	-57%						
6	4.8	1.8	-63%						
7	7.8	3.0	-64%	4.8	7.2	+50%	6.0	6.0	0%
8	4.2	2.1	-50%				6.0	6.0	0%
9	2.7	2.1	-23%	3.6	5.4	+33%	4.5	4.5	0%
10	3.6	3.3	-8%						
11	4.8	4.2	-18%	4.2	6.0	+43%	6.0	5.7	-5%
12	1.5	0.6	-60%				5.4	5.4	0%
16	4.8	4.8	-0%						
18	6.6	3.6	-57%						
19	4.8	3.0	-45%				6.0	6.0	0%

\* Calculated on basis of ten-minute control period preceding distention.

† Calculated on basis of five-minute control period during distention.

‡ Calculated on basis of first ten-minute control period after section of hepatic nerves.

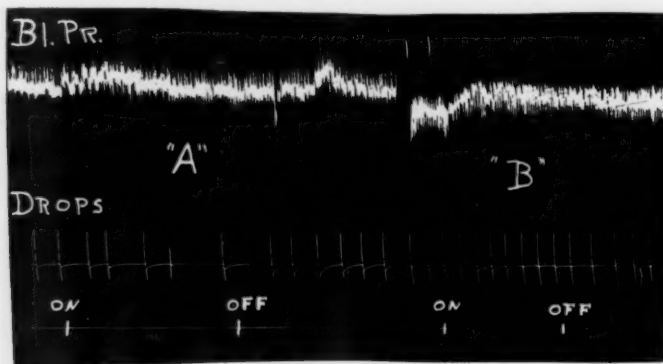
Distention of the entire colon in Dogs No. 4 and No. 18 did not influence bile flow after marked choleresis had been caused by administering 2 cc. of 20 per cent sodium dehydrocholate intravenously. The choleretic stimulus of the injected oxidized bile salt was more powerful than the inhibitory effect of colonic distention, a point which should be of therapeutic significance.

In two dogs, the colon was distended after the vagi were sectioned in the neck, and the same inhibition in bile flow took place. This indicates that the reflex pathway is not resident in the vagi.

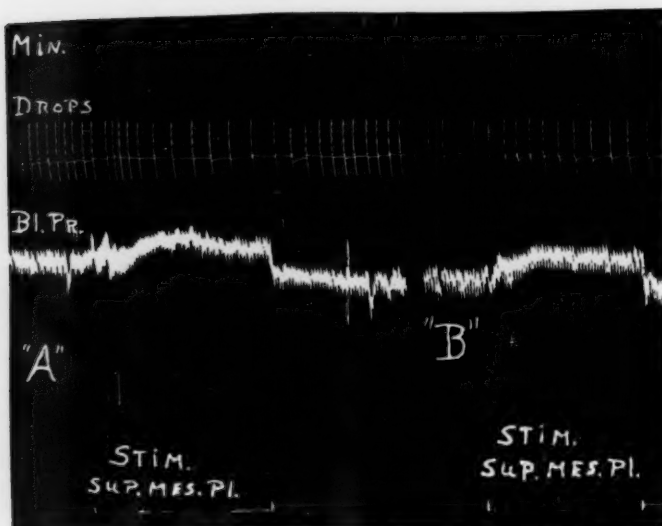
In three rhesus monkeys, the same experiments were carried out in a similar manner and bile formation was uniformly inhibited. Control flows

of 3.0, 4.2 and 3.6 cc. per hour were decreased to 2.0, 3.0 and 2.1 cc. per hour, or —33, —29 and —41 per cent respectively, averaging —34.4 per cent.

*Stimulation of the Central End of Colonic Nerve.*—Stimulation of the splanchnic nerves to the intestinal tract caused a similar inhibition in bile flow from the liver, suggesting that the response from the distention of the



GRAPH 1.—Showing the effect of distention of the colon before, "A," and after, "B," section of the hepatic nerves on bile formation.



GRAPH 2.—Effect of stimulation of the superior mesenteric plexus before, "A," and after, "B," section of the hepatic nerves on bile flow.

colon is due to nervous reflex effect upon the liver. The colonic nerve innervates most of the descending colon and can be found in its mesentery accompanying the caudal or inferior mesenteric artery. Stimulation in four dogs (Table II) caused an inhibition in bile flow ranging from —17 to —79 per cent, averaging —37 per cent. Although this represents the period during stimulation in about one-third of the cases, the inhibition persisted for

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several minutes after the current was interrupted. During the stimulation of the nerves the blood pressure rose from 10 to 80 Mm. Hg. above the control levels. This pressor effect was more marked on nervous stimulation than on distention of the colon.

TABLE II

RESULTS OF EFFECT OF STIMULATION OF COLONIC NERVE ON BILE FLOW  
BEFORE AND AFTER SECTION OF HEPATIC NERVES

Stimulation Colonic Nerves				Section Hepatic Nerves			Stimulation Colonic Nerve After Section Hepatic Nerves			
Dog No.	Control Bile Flow —Cc. Per Hour	During Stimulation	Per Cent Change	Control —Cc. Per Hour	After Section —Cc. Per Hour	Per Cent Change	Control —Cc. Per Hour	During Stimulation	Per Cent Change	
1	3.6	1.5	-79%	7.2	9.0	+20%	7.2	7.2	0%	
17	10.2	8.4	-18%							
19	3.6	2.7	-25%							
24	10.8	9.0	-17%	5.4	6.0	+10%	{ 4.8 3.6	{ 4.2 3.6	{ -12% 0%	
Stimulation Inferior Mesenteric Plexus				Inferior Mesenteric Plexus			Stimulation Inferior Mesenteric Plexus After Section of Hepatic Nerves			
1	3.6	2.4	-33%	6.0	10.2	+62%	{ 6.0 7.2	6.0	0%	
2	3.0	2.1	-30%							
	3.0	1.3	-55%							
5	6.3	3.0	-52%							
19	5.4	2.4	-57%							
	5.4	3.6	-33%							
21	3.6	2.7	-25%	7.2	8.4	+16%	{ 6.3 6.3 4.8 4.2	6.3	{ 6.0 4.8 4.2	{ 0% -5% 0% 0%
22	9.0	6.3	-30%							
23	2.4	1.8	-25%							
26	3.0	2.4	-20%							
							3.9	4.2	+7%	

*Stimulation of the Central End of the Inferior (Caudal) Mesenteric Plexus.*—(A) This group of nerve fibers was sectioned and its central end stimulated with a shielded electrode just cephalad to the juncture where the twigs from the superior hemorrhoidal fibers join the colonic nerve. Ten stimulations in eight dogs were associated with a —20 to —57 per cent inhibition of bile flow, or an average of —36 per cent (Table II).

Four stimulations in three monkeys reduced the control flows of 3.6, 3.6,

3.0 and 3.0 cc. per hour to 2.4, 2.7, 2.4, and 1.8 cc. per hour, or —33, —25, —20 and —40 per cent, respectively, the average reduction being 30 per cent.

*Stimulation of the Central End of Superior (Caudal) Mesenteric Plexus.*—(B) This group of nerve fibers supplies the small intestine and part of the proximal colon. They were freed from the superior mesenteric artery in the root of the mesentery of the small bowel divided and enclosed in a shielded electrode. Stimulation of this plexus caused a slowing of from 33 to 53 per cent, or an average inhibition of 38.7 per cent (Chapter 2, Table III), in bile formation.

TABLE III

RESULTS OF EFFECT OF STIMULATION OF SUPERIOR MESENTERIC PLEXUS ON RATE OF BILE FLOW BEFORE AND AFTER SECTION OF HEPATIC NERVES

Dog No.	Stimulation Superior Mesenteric Nerves			Section Hepatic Nerves			Stimulation Superior Mesenteric Nerves After Section Hepatic Nerves		
	Control Bile Flow —Cc. Per Hour	During Stimulation —Cc. Per Hour	Per Cent Change	Control —Cc. Per Hour	After Section —Cc. Per Hour	Per Cent Change	Control —Cc. Per Hour	During Stimulation —Cc. Per Hour	Per Cent Change
25	5.4	3.6	—33%	3.6	1.6	+25%	3.0	3.0	0%
32	9.0	4.2	—54%	3.0	4.8	+38%	3.6	3.6	0%
33	3.6	1.8	—50%				6.6	6.6	0%
34	7.8	4.8	—38%				6.6	6.0	—9%
							6.6	6.6	0%

*Distention of Urinary Bladder.*—The urinary bladder was distended in three dogs by injecting 125 to 200 cc. of tap water at 40°C. (Table IV). An inhibition in bile flow of —30, —40 and —40 per cent, averaging —37 per cent, was observed. It has been noted during many bile-flow experiments that there was usually an acceleration in bile flow during spontaneous micturition, without any associated alteration in blood pressure. This agrees with the observations just mentioned.

*Stimulation of the Central End of the Pelvic Nerve.*—The pelvic nerve was stimulated once in two dogs and twice in two other dogs. A diminished bile flow of from —30 to —45 per cent, or an average of —37 per cent, resulted (Table IV).

*Section Hepatic Nerves, Followed by Distention of Colon and Stimulation of Nerves.*—Nearly all the nerve supply to the liver surrounds the hepatic artery near the hilum and comprises a rich plexus of fibers, which together often almost equals the size of the artery itself. This plexus is made up predominantly of splanchnic fibers which spread from the celiac plexus along



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the arterial pathways. It also contains branches from the right vagus and a few fibers from the left vagus nerves. Occasionally a small group of fibers may be seen on the adventitia of the portal vein.

The nerves were dissected free from the hepatic artery near its origin and sectioned. There was an immediate augmentation of bile flow from 10 to 70 per cent, averaging 36 per cent. A drop in general blood pressure usually followed this procedure, although it returned to a normal level after a few minutes. This confirms the observations made by Tanturi and Ivy<sup>14</sup> and provides additional evidence that the hepatic nerves in some way regulate bile secretion.

TABLE IV  
RESULTS OF EFFECT OF DISTENTION OF URINARY BLADDER ON BILE FLOW  
BEFORE AND AFTER SECTION HEPATIC NERVES

Dog No.	Distention of Bladder			Section Hepatic Nerves			Distention of Bladder After Section Hepatic Nerves		
	Control Bile Flow —Cc. Per Hour	During Distention	Per Cent Change	Control —Cc. Per Hour	After Section —Cc. Per Hour	Per Cent Change	Control —Cc. Per Hour	During Stimulation	Per Cent Change
2	3.0	2.1	-30%						
5	6.0	3.6	-40%						
6	6.0	3.6	-40%						
11							6.0	6.0	0%
	Stimulation Nerve Erigens						Stimulation Nerve Erigens After Section Hepatic Nerves		
28	3.0	2.1	-30%	3.6	6.0	+40%	3.6	3.9	+9%
	5.4	3.0	-40%				4.2	4.2	0%
29	5.4	3.6	-33%	4.2	9.0	+54%	4.5	4.2	-7%
30	9.0	6.0	-33%	7.2	9.6	-33%	7.8	7.2	-8%
							9.6	9.0	-7%
31	5.4	3.0	-45%	7.2	8.4	+16%	6.6	6.0	-10%
	5.4	3.3	-39%				7.2		
							7.2	6.6	-8.9%

When the colon was redistended after section of the hepatic nerves in four dogs, there was little or no change in bile flow; the changes varied from 0 to -10 per cent, or averaged -0.8 per cent (Table I). The colonic nerve was restimulated three times in two dogs; no change occurred in two instances, and -12 per cent change occurred in the remaining dog (Table II). Stimulation of the inferior mesenteric plexus, a total of seven times in three dogs, was followed by alterations of +7 to -5 per cent from the control

flow, the average changes being  $+0.8$  per cent (Table II). Five stimulations in two dogs resulted in no change when the superior mesenteric plexus was stimulated after section of the hepatic nerves, except a  $-9$  per cent decrease on one occasion. Similar results are noted in Table IV when the bladder was redistended or the pelvic nerve restimulated after section of the hepatic nerves.

It is obvious from these results that the integrity of the hepatic nerves is essential for the observed inhibition of bile formation when the colon or bladder is distended or when the mesenteric nerves are stimulated. This proves the inhibition is due to a nervous reflex mechanism. The slight inhibition in flow after section of the hepatic nerves in a few cases suggests that some of the fibers may not have been divided.

In seven dogs whose blood pressure was below 60 Mm. Hg., inhibition of bile flow did not take place when the colon was distended or its nerve supply stimulated, and in three of this group there was a slight increase in the rate of flow. The dog's general condition was either so poor that the normal reflex response could not be elicited or the resultant increase in blood pressure improved the circulation through the liver so as to augment its bile secretion.

Acholia, associated with a markedly congested liver, developed in one dog during the course of the experiment. The bile flow did not become reestablished after the intravenous administration of sodium dehydrocholate. The common duct was not kinked.

Observations during the experiments, as well as other work on acute biliary fistula animals, suggest that the concentration or viscosity of the bile varies inversely with the rate of flow. When the flow from the liver increased the concentration decreased, which would produce a thicker bile that might favor precipitation of its constituents and flow more slowly through the bile passages.

*Discussion.*—The mechanism of this reflex response involves an analysis of the known effects of stimulation of the nerve supply to the liver, particularly in connection with bile formation. Stimulation of the hepatic or splanchnic nerves causes definite vasomotor changes in the liver. Bayliss and Starling,<sup>15</sup> Francois-Franck and Hallion,<sup>16</sup> Burton-Opitz,<sup>17</sup> and Bauer, Dale, Poulson and Richards<sup>18</sup> observed an increase in blood pressure in both the hepatic artery and the portal system on stimulation of these nerves. A decrease of liver volume signifying vasoconstriction within the liver accompanied this stimulation and occasionally persisted after the stimulus was interrupted. Burton-Opitz<sup>19</sup> showed that there is a diminished blood flow through the liver, and concluded that the arterial and portal vasomotor mechanisms are separate and do not depend one upon the other. Olds and Stafford,<sup>20</sup> later, found by injection methods that the terminal branches of the hepatic artery and portal vein separately communicate with the hepatic sinusoids, thereby placing the above physiologic observation on an anatomic basis as well.

Lundberg<sup>21</sup> and Hillyard<sup>22</sup> sectioned the nerve supply to the liver in chronic biliary fistula dogs and reported no change in the output of bile. Tanturi and Ivy,<sup>14</sup> in acute experiments, recently observed an augmentation of bile flow following section of the splanchnic or hepatic nerves and an inhibition when the distal ends of these nerves were stimulated, providing evidence that the rich nerve supply to the liver has some control over the secretion of bile.

The following possibilities may be offered to explain the inhibitory reflex effects on bile flow brought about by stimulation of the nerves mentioned above: (a) Constriction of the intrahepatic biliary channels, thereby obstructing the flow of formed bile; (b) kinking of the bile canaliculi which form a diffuse network around the portal branches; (c) contraction of Glisson's capsule; (d) by constriction of the intrahepatic veins, thereby increasing the intrahepatic pressure to such a point that it would overcome the relatively low pressure (25 to 30 cm. bile) in the bile channels; (e) changes in the minute blood flow through the liver; and (f) the presence of inhibitory-secretory fibers in the splanchnic nerves to the liver.

Constriction or kinking of the interlobular bile ducts, as a result of splanchnic nerve stimulation, is unlikely because the period of inhibition should then be followed by a period of increased flow due to the release of temporarily obstructed bile. This does not occur. Contraction of Glisson's capsule could explain the observations on a pressure basis.

Heidenhain<sup>23</sup> and Murk<sup>24</sup> believed from their observations that changes in blood flow affect bile formation. The increase in blood flow through the portal system following a meal<sup>25</sup> or bile salt injection<sup>26</sup> is associated or followed by an increased flow of bile from the liver. The choleresis reported by the local or general application of heat<sup>27</sup> is associated with increased blood flow. The inhibition of bile flow on splanchnic stimulation is associated with an inhibition in blood flow through the liver. Tanturi and Ivy<sup>14</sup> found that the increased blood flow is associated with increased bile flow as long as it does not increase the intrahepatic pressure.

The fibers of the vagi have been found to exert an excitatory or inhibitory secretory effect in dog and monkey.<sup>28</sup> It is likely that the splanchnic nerves contain inhibitory-secretory fibers. However, it would be difficult to prove the presence of such fibers in the hepatic nerves since they exert such a marked effect upon hepatic circulation. The augmentation of bile flow following section of the hepatic nerves is only indirect and equivocal evidence that inhibitory fibers are being sectioned even though this response often continues after the blood pressure has risen to its normal level.<sup>14</sup>

The inhibition of bile flow from the liver due to nervous impulses from the colon in the dog and monkey offers proof of reflex pathways from the bowel to the biliary system and suggests that a diminished amount of a thicker bile may be elaborated. If this stasis in bile flow were continued by repeated stimuli from the colon, precipitation of calculi might be favored, and difficulties in the flow of bile through the ducts might result. Obviously,

it would be of interest to determine whether the same mechanism could be shown to exist in man. There is no reason, however, to doubt the existence of the mechanism in man.

## CONCLUSIONS

(1) Distention of the colon in the dog and monkey caused an inhibition in the flow of bile from the liver. This distention had no effect on the bile flow when choleresis had been established by the injection of sodium dehydrocholate.

(2) A similar response following stimulation of the central end of the colonic, inferior mesenteric, superior mesenteric nerves and pelvic nerve indicates that this inhibition is of reflex origin. Section of the hepatic nerves is followed by an increase in bile flow and prevents the above effects.

(3) The possibility of inhibitory-secretory fibers in the splanchnic or hepatic nerves and the effect of alterations in the blood flow caused by excitation of these nerves on bile formation are two factors which may explain, in part, the reflex inhibition of bile formation that occurs on the stimulation of the afferent mesenteric nerves.

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## CIRCULATORY PROBLEMS OF SURGICAL IMPORTANCE IN THE DIAGNOSIS OF ABDOMINAL LESIONS\*

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MOST of the papers presented before the American Surgical Association on the subject of cardiovascular disease naturally feature the results obtained from direct surgical attack in its relief. It seemed to us it might be worth while to discuss certain problems presenting difficulties in differential diagnosis and, therefore, in the proper management of various types of cardiovascular lesions which have confused surgeons from time to time in distinguishing them from the acute surgical abdomen. We cannot lay claim to originality in recognizing these difficulties. All of these problems have been met with before, but in isolated case reports, and so we hope that it might serve a useful purpose to group them into one working classification. Our object, therefore, in presenting this paper is to again stress these diagnostic pitfalls which we must avoid in distinguishing between the so-called acute surgical abdomen, demanding immediate operative interference, and instances of cardiovascular disease *equally demanding* that operative intervention shall be withheld. It has proved to be most helpful to us in estimating the surgical risk to classify our cases with surgical lesions complicated by cardiovascular handicaps according to a grouping of such risks published by us in a previous paper.<sup>1</sup> Now, based upon the combined experiences of the Departments of Surgery and Cardiology at the Woman's Medical College Hospital, and more particularly upon that of the latter department, of the last eight years in the study of 4,083 cases, we wish to classify the types of cardiovascular disease giving rise to abdominal symptoms and to briefly cite cases illustrative of each type occurring in our services (Table I).

*Mode of Production of Symptoms.*—Abdominal symptoms may be produced by almost any of the etiologic types of heart disease. The mechanism of the production of the symptoms, however, is variable. For example, the failure of the heart as a pump causing congestion of the abdominal organs is usually first reflected in enlargement of the liver. Rheumatic heart disease with mitral stenosis is to be suspected in over 50 per cent of these cases. However, hypertensive or arteriosclerotic heart disease may be the causative agent. Continued untreated congestive cardiac failure may produce symptoms usually encountered in gastro-intestinal tract disease—gas, anorexia, nausea, vomiting, diarrhea, fulness and pain in the abdomen, and loss of weight. Mild, yet clinically detectable, degrees of jaundice may be added to the symptom of right upper quadrant pain caused by sudden distention of

\* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

# SYMPTOMATOLOGY OF VASCULAR PATHOLOGY

TABLE I

CLASSIFICATION OF CIRCULATORY DISTURBANCES OCCASIONALLY PRODUCING ACUTE  
ABDOMINAL SYMPTOMS

- (1) Cardiac Failure
  - (A) Congestive Type
    - Liver Enlargement (right upper quadrant pain).
    - G.-I. Tract Congestion (nausea, vomiting, gas, hemorrhage, *etc.*).
  - (B) Coronary Type (reflex)
    - Angina (pain referred to upper abdomen).
    - Coronary Occlusion (similar mechanism).
- (2) Pericarditis
  - (A) Acute Pericarditis (pain at times referred to abdomen).
  - (B) Calcific Pericarditis (cardiac compression. Ascites may be an early symptom).
- (3) Embolism and Thrombosis
  - (A) Mitral Stenosis (auricular fibrillation). Emboli from large left auricle to splenic, renal, superior mesenteric and inferior mesenteric arteries.
  - (B) Subacute Bacterial Endocarditis (infected emboli from the left side of the heart. Same locations as above).
- (4) Organic Vascular Change
  - (A) Aortic Aneurysm
    - (a) Symptoms produced by tumor growth.
      - Displacement of organs.
      - Vertebral erosion.
    - (b) Symptoms produced by rupture or dissection.
  - (B) Arteriosclerosis. Spasm (abdominal angina).
    - Hemorrhage (in hypertension).
    - Thrombosis.

the liver capsule, completing the masquerade.<sup>2</sup> Ascitic fluid in small amounts may arise to further complicate the picture.

In certain types of heart disease, embolism is a frequent mode of production of confusing abdominal symptoms. Again, patients with mitral stenosis and enlargement of the left auricle constitute the majority of this group. Subacute bacterial endocarditis, with its tendency to involvement of the left side of the heart, is likewise a dangerous threat to the integrity of the arterial circulation below the diaphragm. Emboli in vessels supplying the abdominal organs may be responsible for the sudden onset of symptoms simulating a variety of surgical lesions. Occlusion of the mesenteric vessels presents a picture often diagnosed intestinal obstruction. A renal haven for the embolus simulates calculus while a splenic point of rest may give a sudden pain high up in the left quadrant of the abdomen simulating a ruptured viscus.

Referred pain from coronary artery disease with angina, or more frequently occlusion, may simulate any type of gastro-intestinal tract disturbance. The initial studies of Head<sup>3</sup> and Mackenzie<sup>4</sup> have, in recent years, been amplified in monographs by Capps<sup>5</sup> and Jones.<sup>6</sup> The mechanism of pain of the referred type is too well known to need any particular comment here. The abdominal areas of expression in cases of angina and occlusion, and infrequently in cases of acute pericarditis, may simulate gallbladder disease, ulcer or acute pancreatitis. A reversed pathway may explain changes in the cardiac rhythm and even in the form of the electrocardiogram, although the

change arises from a gallbladder focus. Recent experiments upon dogs by Owen,<sup>7</sup> and Crittenden and Ivy<sup>8</sup> have served to prove that this mechanism is more than a mere possibility. Stimulation of the vagus nerve by disturbances in the gallbladder is no doubt the fundamental cause.

Palpable abdominal masses due to aneurysmal dilatations of the abdominal aorta, particularly when they occur in women, are puzzling to the surgeon. Rupture or dissection of the aneurysm produces an acute picture rarely correctly diagnosed and often leading to an unnecessary celiotomy. Smaller hemorrhages, although productive of the same degree of confusion, may occur in abdominal organs in hypertension. Arteriosclerosis of the abdominal vessels may lead to thrombosis, and the clinical picture will depend upon the size and location of the vessels involved. Reduction of the blood supply in

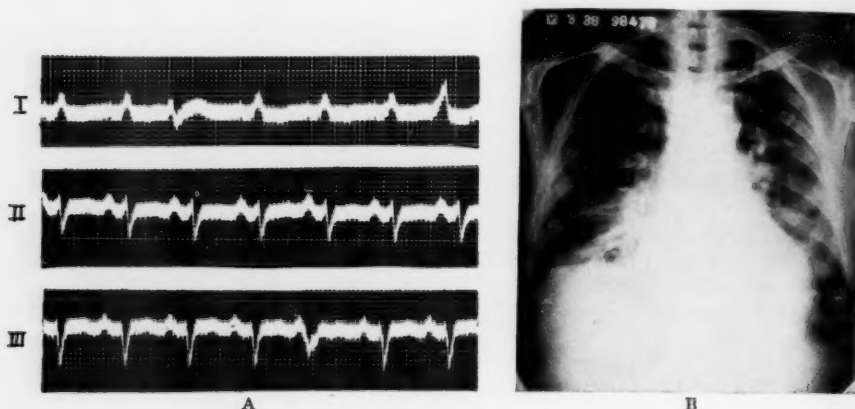


FIG. 1.—Case 1: (A) The electrocardiogram shows evidence of myocardial damage in QRS changes. (B) Roentgenogram shows cardiac enlargement of the hypertensive type.

the absence of thrombotic occlusion may give rise to abdominal symptoms that have been grouped under the clinical head of abdominal angina. Lack of proper blood supply (ischemia) when the demand on the gastro-intestinal tract is greatest (after meals) produces pain.

#### ILLUSTRATIVE CASES

**Case 1.**—Right upper quadrant pain due to enlargement of the liver from cardiac failure simulating gallbladder disease.

Hosp. No. 2136: A. C., a physician, age 63, was admitted to the hospital, with chief complaint of right upper quadrant pain of two weeks' duration. Following a respiratory infection the patient experienced pain followed by anorexia, nausea, occasional vomiting and a slight tint of icterus. There was dyspnea present which he attributed to persisting cough.

Examination showed normal temperature, pulse 116, respiration 22, and blood pressure 122/80. The liver was large and tender. Râles were heard at the lung bases and the heart was enlarged to percussion 2 cm. to the left of the M.C.L. The heart sounds were distant and a soft apical systolic murmur was heard. The rhythm was regular. There was no edema. Roentgenologic examination of the chest (Fig. 1) confirmed the presence of cardiac enlargement, and electrocardiographic study pointed also to the primary cardiac origin of the abdominal symptoms. Blood count, Wassermann and urine were negative. The icterus index was 18.

*Discussion.*—Cases of this type are not at all uncommon. It is interesting to note that this patient was a physician who interpreted the symptoms of right upper quadrant pain, nausea, vomiting and slight icterus entirely in the light of gallbladder disease and requested admission to a surgical service. The upper respiratory tract infection no doubt was the immediate cause of the upset, and the patient explained his dyspnea and cough entirely on this basis. The rapid onset of the right-sided cardiac failure caused marked engorgement of the liver with stretching of the capsule; this focused attention on the gallbladder as a primary source of the trouble due to the localized pain and tenderness. The other gastro-intestinal symptoms were produced by stasis of blood in the areas drained by the portal circulation. Even hemorrhage at times can occur in these cases with long-standing congestion due to ulceration in the devitalized areas of mucosa.

Symptoms of this type in patients in the younger age groups are generally due to advanced mitral stenosis and are then less apt to be confused with the symptoms of gallbladder disease.

Bed rest and rapid digitalization in this case promptly resulted in improvement in the gastro-intestinal symptoms. The liver diminished in size and the tenderness disappeared. Some weeks later the patient began to experience attacks of paroxysmal cardiac dyspnea (cardiac asthma), nocturnal in type, giving further evidence of the true nature of the underlying process.

An interesting fact in this case was the complicating jaundice. Rarely can this symptom occur in such a marked degree in the absence of true disease of the digestive apparatus. Retention of bilirubin here was sufficient to impart a distinct tint to the skin and sclerae. The congestive failure impaired the excretory function of the liver, since an organ suffering from the effects of so marked an anoxemia is unable to excrete a larger amount of bile pigment. The nutmeg liver, the term applied to the organ in this condition, shows on microscopic section compression of the central cells of the liver lobule.

At times, especially in mitral stenosis, jaundice may suddenly appear following a pulmonary infarction. Although this was first believed to be caused by the extra load of hemoglobin capable of breaking down and producing excess bilirubin, it has since been shown to be due to the intensification of the anoxemia of the liver cells following the infarction.

The investigations of Rich and Resnick<sup>11</sup> support this view. Kugel and Lichtman,<sup>10</sup> more recently, in an analysis of clinical and pathologic material, studied all aspects of the subject and advanced the following explanation for the frank jaundice seen in cardiac failure of the type described in Case 1:

"In a patient with a long standing pulmonary stasis due to cardiac insufficiency, pulmonary infarction occurs. From this rich source, hemoglobin is made available by destruction and hemolysis of red blood cells and bilirubin is rapidly formed. The presence of serum in the lung, owing to the congestion and often to infection, facilitates the solution and absorption of the bilirubin. The capacity of the liver to excrete the substance is impaired owing to the anoxemia and to the toxic effect of infection on the parenchyma of the liver.

However, unless extensive disease of the liver, *i.e.*, true cirrhosis, is present, the causation of the frank jaundice is primarily pulmogenic. The deleterious effects of anoxemia and of infection on liver cells play a necessary but only a secondary rôle. The pulmonic factors of primary importance are the duration and type of the heart failure, *i.e.*, prolonged failure of or obstruction in the left side of the heart and pulmonary congestion and the local factors favoring the rapid formation and absorption of bilirubin, *i.e.*, pulmonary infarction, hemolysis of erythrocytes and local or systemic infection."

**Case 2.**—Abdominal pain and liver enlargement followed by ascites due to calcific pericarditis causing cardiac compression.

Hosp. No. 1325: R. F., age 12, was admitted to the hospital, complaining of abdominal pain and tenderness and increase in abdominal size of three years' duration. There was dyspnea and, lately, pretibial edema. The past history was negative for rheumatic infection. Examination showed a blood pressure of 90/60, a systolic apical murmur and little or no increase in cardiac size. There was noted distention of the jugular veins (venous pressure 240 Mm.). Marked ascites was present. Fluoroscopy showed a small, quiet heart and oblique roentgenogram of the heart demonstrated the presence of an encasing shell of calcium.

**Discussion.**—In this patient, deposits of calcium about the heart caused compression and faulty diastolic filling; these were responsible for the presenting abdominal symptoms. The diagnosis was suspected when studies revealed a small, quiet heart, a rising venous pressure, and a falling systemic pressure. Attention was directed away from the abdomen, and thoracic surgery was advised to relieve the symptoms of cardiac compression.

Acute pericardial processes, particularly in children, may be accompanied by pain referred to the abdomen. In some cases acute inflammation of the appendix may be suspected and operation performed. Pain in acute pericarditis usually results from extension of the inflammatory process to the mediastinum or to the diaphragmatic pleura. This type of pain may give abdominal reference but careful study of the heart should reveal the true underlying cause. Detection of the characteristic pericardial friction rub many times serves to clear the diagnosis. When the process extends to the diaphragm, cough and deep breathing accentuate the pain and this is important in the differential diagnosis. The pericarditis met in terminal conditions like nephritis never gives pain referred to any abdominal area due to the absence of the complicating pleuropericarditis. In one patient in our series, abdominal pain was found to be caused by acute rheumatic pericarditis. A second attack a few weeks later, accompanied by rectus rigidity, was proved to be due to rheumatic involvement of the appendix, the appendix on section showing typical Aschoff bodies.

**Case 3.**—Coronary sclerosis followed by acute coronary occlusion, diagnosed gallbladder disease.

Hosp. No. 763: N. M., male, age 51. When first seen this patient complained of indigestion and gas and occasional pain over the right upper abdomen. Dyspnea and palpitation had been experienced for some years. No edema or chest pain. The significant findings were overweight, slight increase in blood pressure (163/92), occasional pre-



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mature beats, but not much increase in heart size. The electrocardiogram (Fig. 2 A) showed only a left axis deviation. The patient was placed on a dietary regimen and told to make arrangements for a gallbladder roentgenologic study. This he failed to do, and when next seen, four months later, he showed no improvement. The indigestion was worse, the dyspnea was increasing, and he stated that a week before the second examination he had experienced a very severe attack of indigestion. This attack came on at night, awakened him from his sleep, and required a hypodermic injection of morphine for relief. Another electrocardiogram (Fig. 2 B) showed the presence of a recent coronary occlusion of the posterior type.

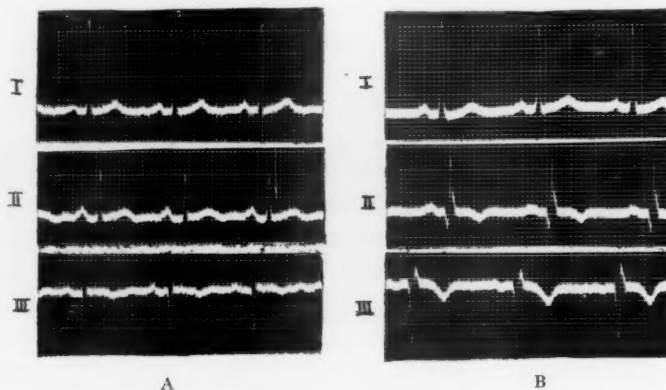


FIG. 2.—(A) Electrocardiogram on first examination shows only a left axis deviation. (B) Second tracing showing presence of coronary occlusion of posterior type.

*Discussion.*—Differential diagnosis in this type of patient is usually more difficult. Many times, in patients of this age and build, it is not infrequently discovered that gallbladder disease and coronary disease coexist. This has led to a great deal of discussion and much speculation in the literature. The exact relationship between a diseased gallbladder and the heart remains a complex subject although convincing electrocardiographic evidence of improvement has at times been observed to follow cholecystectomy.<sup>13</sup> Many investigators have also demonstrated the existence of important reflex pathways between the gallbladder and the heart. Even effects upon the cardiac rate and rhythm have been shown to occur at the time of operation. It has been our impression in a number of these cases, where striking postoperative improvement in the pain has been observed, that our initial opinion as to the degree of coronary involvement was incorrect. In other words, most of the symptoms were produced by disease in a high lying gallbladder.

Our chief concern, therefore, lies in the correct identification of the major lesion. The pain of acute coronary occlusion is often confused with the pain produced by gallstones and a celiotomy performed.<sup>14, 15, 16</sup> Pain, vomiting, fever, and leukocytosis are commonly met with in both conditions. However, if the past history is carefully reviewed, the patient with gallbladder disease will usually be found to have a history of indigestion, while the patient with coronary occlusion may give a history of mild attacks of angina resulting from effort. A complete cardiac study, using the form suggested by us,<sup>1</sup> will

seldom fail to throw considerable light on the correct diagnosis. In Case 3, the second electrocardiogram furnished the diagnosis and localized the infarction (Fig. 2 B). The characteristic T-wave changes were seen. The degree of shock observed in coronary occlusion is not present in gallbladder disease nor is the sharp drop in the blood pressure so constant in gallbladder colic as it is in coronary occlusion. The appearance of a friction rub over the precordium in cases of anterior coronary occlusion clinches the diagnosis in favor of occlusion while the appearance of jaundice swings the balance toward gallbladder disease.

Cholelithiasis may cause, reflexly through the autonomic nervous system, certain changes in the rhythm of the heart.<sup>17</sup> Babcock<sup>18</sup> believes that inhibition of the heart can be caused by stimulation of the filaments of the vagus

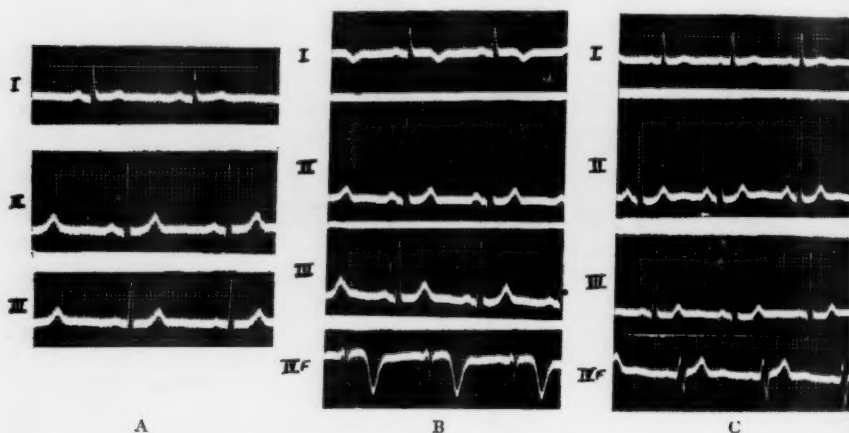


FIG. 3.—(A) Electrocardiogram on admission shows little change. (B) Taken eight hours after A. Note change in T<sub>1</sub> and T<sub>4</sub> indicative of anterior coronary occlusion. (C) Showing return of the electrocardiogram to normal eight months later.

arising from the wall of the gallbladder. Heart block, relieved by atropine, has been reported to result from gallbladder stimulation. The jaundice produced in some patients by gallbladder disease may secondarily affect the cardiac mechanism. Systolic apical murmurs have been reported, by some observers, appearing during pain from a gallbladder focus. Consequently the only reliable electrocardiographic evidence in the differential diagnosis lies in the T-wave alterations seen in the patient we have presented.

**Case 4.**—Coronary sclerosis followed by acute coronary occlusion diagnosed ruptured peptic ulcer.

Hosp. No. 4027: J. M., male, age 50, was admitted to the College Hospital, July 6, 1938, with chief complaint of sudden, severe epigastric pain coming on while at work. He gave a history of two years' treatment for gastric ulcer. No roentgenologic study, however, had been made. When first seen, the patient was pale, sweating. Pulse 100, temperature 97° F., respiration 30. The heart was not enlarged, blood pressure 100/70. There was upper abdominal tenderness, but no marked rigidity. W.B.C. 12,000. The first electrocardiogram was negative. The pain was completely relieved following injection of  $\frac{1}{4}$  gr. of morphine. A second electrocardiogram taken a few hours later showed marked change (Figs. 3 A and B).

*Discussion.*—The previous history of digestive disturbance complained of by this patient was no doubt caused by his cardiac lesion. He presented this vague type of "indigestion" for some years. Although he was never fully studied to prove the diagnosis of peptic ulcer before he was seen by us, it was assumed that the lesion was present due to the favorable effect of alkali therapy in improving the indigestion and "gas." The history of this type of treatment centered the attention at the time of the attack on the gastro-intestinal tract, and the erroneous diagnosis of ruptured peptic ulcer was made in the receiving ward and the patient placed on a surgical service. It is a matter of additional interest that the usual leads of the first electrocardiogram were entirely negative. As is many times the case, the typical electrocardiographic changes did not develop entirely until 18 hours after the onset of the attack. The second tracing shows characteristic changes in leads 1 and 4. At the same time a friction rub was heard over the precordium, clinching the diagnosis. It appears, then, that the dangerous period for the patient is the silent interval between the onset of the attack and the development of pathognomonic electrocardiographic and physical signs. This patient made a prompt and uneventful recovery. On March 11, 1939 (Fig. 3C,) evidence of the accident had disappeared from all leads of the electrocardiogram. Subsequent roentgenologic studies failed to reveal an ulcer.

**Case 5.**—Abdominal aortic aneurysm of arteriosclerotic origin simulating acute surgical abdomen at time of dissection prior to final rupture.

Hosp. No. 3784: F. E., male, age 68, had been healthy, except for occasional attacks of indigestion, until the sudden onset of a tearing pain in the upper abdomen with radiation to the right lumbar region. It was accompanied by sweating, pallor and vomiting, and when the patient attempted to go to the bathroom, the slight exertion caused him to fall to the floor in collapse. There was involuntary emptying of the bladder and bowel. When first seen, he was pulseless with rapid shallow respirations. The picture was one of impending dissolution. The abdomen showed a board-like rigidity and the temperature by rectum was 95° F. In 20 minutes, the patient regained consciousness and the pulse became perceptible at the wrist. He complained of pain in the upper abdomen and vomited again. A diagnosis of perforated peptic ulcer was made and operation advised. Further observations changed this diagnosis when the patient quickly improved and the board-like rigidity of the abdomen disappeared. A mass, thought to be an aneurysmal sac, was palpated and on account of continued abdominal pain, the patient was given large doses of morphine and placed on shock treatment. The patient showed rapid improvement in blood pressure, color and pulse volume for 36 hours. At the end of that time there was a recurrence of severe abdominal pain, again accompanied by signs and symptoms of profound shock. Board-like abdominal rigidity did not recur and the aneurysmal sac was distinctly felt. It was more tender and larger in size and there was a bulging in the right flank. The patient showed marked pallor, and gave no response to the usual measures. He died in coma in two hours.

*Autopsy* showed no peptic ulcer, but advanced atherosclerosis of the aorta, an abdominal aortic aneurysm with rupture. The entire right side of the abdomen from the spinal column to the lateral wall and from the liver to the pelvis was filled with massive retroperitoneal blood clot that had pushed the posterior peritoneum so far forward that it was nearly in contact with that of the abdominal wall (Fig. 4). The hemorrhage had

pushed into and split the mesentery of the cecum and ascending colon. The mesentery of the small bowel was not affected. The kidney, ureter, adrenal gland and other retroperitoneal structures floated in the enormous clot.

*Retroperitoneal Space and Structures.—Aorta:* The wall was thin and inelastic, and the intima was pitted and cracked with atheromatous ulcers. Just distal to the origin of the superior mesenteric artery, extending to and involving the bifurcation, was a large, fusiform dilatation which projected forward and to the left into the abdomen. After removal this measured 14x8x6 cm. The root of the mesentery lay across its anterior sur-

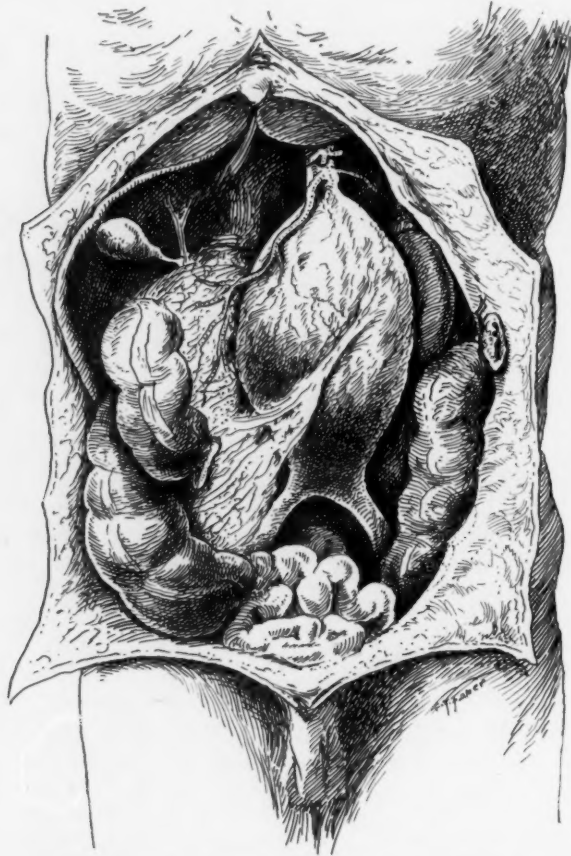


FIG. 4.—Drawing showing relationship of aneurysmal dilatation to surrounding structures. (Reprinted from New International Clinics, 1, Series 2; through courtesy of J. B. Lippincott Co.)

face. When opened, the forward bulging portion was found to be filled by layers of dense yellow fibrin. The wall was continuous with that of the aorta, overlaid and reinforced by peritoneum and its connective tissue, to which it was closely adherent. The lumen of the vessel, which went through the mass against the posterior wall, was lined by a smooth, red layer of fresh thrombus. In the central portion of this thrombus was a small fissure which overlaid a short (1 cm.) irregular rupture in the posterior wall of the vessel.

*Discussion.*—Abdominal aortic aneurysm is a rare although extremely important lesion to keep in mind in connection with circulatory problems that figure in the differential diagnosis of abdominal lesions. Symptoms from its

rupture or dissection often confuse the surgeon in the diagnosis of abdominal emergencies, puzzle the urologist, when small hemorrhages invade the tissues about the kidney or press on the ureter, and frequently tax the diagnostic acumen of both internist and neurologist in interpreting pain referred to various sections of the body.

It is surprising how large abdominal aneurysms may become and how great a displacement of the abdominal organs they may cause and still elude clinical detection if the sac points posteriorly and does not erode the vertebrae. Thompson<sup>19</sup> reported an abdominal aneurysm, in a laborer, age 39, which contained six and one-half quarts of fluid blood and clots at autopsy. This aneurysm had pushed both kidneys so far forward that they were diagnosed as metastatic masses on palpation. This patient had not consulted a physician until the last few weeks of life. Many cases reported in the literature were not seen until they had become moribund following perforation or dissection. When subjective symptoms from these cases are tabulated, the most frequently recorded is pain. It may be of any variety from a vague type of abdominal discomfort, occurring at times in patients before rupture, to the typical, agonizing terminal variety of pain attending the tearing of the aortic wall. The type of pain experienced by the patient in these vascular accidents is outstanding. Extremely large doses of morphine seem ineffective in such calamities and these circumstances alone should always suggest an abdominal vascular complication. The ensuing symptoms of profound shock add further evidence. Many times, in the cases reported in the literature and in our case, preliminary smaller ruptures precede the final event. The intermittent hemorrhages confuse the picture and often unnecessary surgical exploration is undertaken. The distribution and character of the pain at the time of rupture depend on the location of the aneurysm and the point of rupture. Extravasations into the retroperitoneal space (Case 5) are frequent. If either kidney or the ureter is involved, renal colic is simulated and the pain may radiate down the inner aspect of the thigh to the testicle. The high site of the rupture, as in this case, often leads to the diagnosis of ruptured peptic ulcer.<sup>22,23</sup> This was the impression of the first physician to reach the patient's side. Vomiting and diarrhea are frequently present and serve to further complicate the picture.

Figure 5, compiled from cases reported in the literature, shows the variety of symptoms that may result from rupture, pressure or dissection when various structures of the body are involved:<sup>24</sup> (1) Retroperitoneal rupture with perinephric collection simulating abscess;<sup>25, 26, 27</sup> (2) pressure on ureter with picture of uremia;<sup>28</sup> (3) rupture into the gastro-intestinal tract (duodenum<sup>29, 30, 31, 32</sup>)—pressure on duodenum gives symptoms of pyloric obstruction;<sup>33</sup> (4) rupture into the peritoneal cavity;<sup>34</sup> (5) rupture simulating psoas abscess;<sup>35</sup> (6) dissection with pressure on iliac arteries followed by gangrene;<sup>36, 37</sup> (7) rupture through the diaphragm into the pleural cavity with symptoms of thoracic disease;<sup>38</sup> (8) spinal erosion with pain in the back and legs;<sup>39</sup> and (9) rupture into the inferior vena cava (arteriovenous aneurysm). Consequently, abdominal aneurysms may produce melena, hemoptysis or



hematemesis. Portal, splenic or mesenteric vein thrombosis may occur and give the first clue to the presence of an aneurysm.<sup>40, 41</sup>

The clinical diagnosis of abdominal aortic aneurysm rests upon the demonstration of a pulsating, expansile tumor mass.<sup>42</sup> This sign was present at the time of the second examination of Case 5. Inspection in this case showed a very slight anterior bulge of the abdominal wall but no pulsations could be seen. At times a thrill may be palpable over the suspected mass. Palpation, carefully carried out, usually clinches the diagnosis. The tumor mass, when

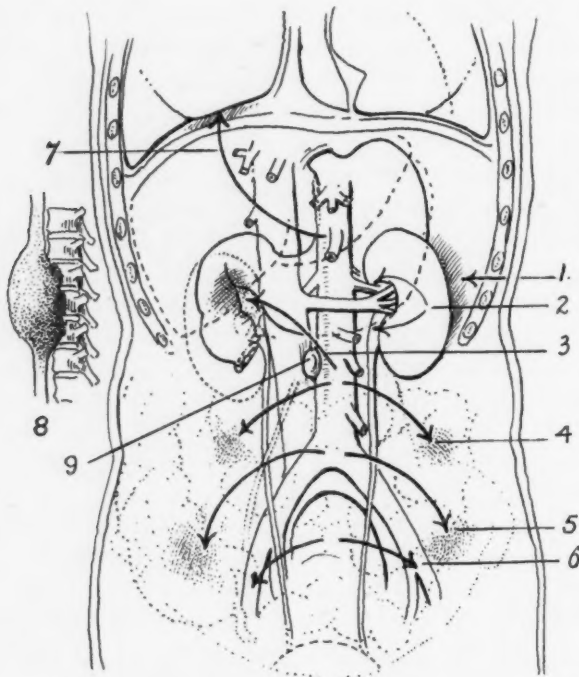


FIG. 5.—Diagram showing organs involved and pathways of dissection in reported cases of ruptured abdominal aortic aneurysms. (Reprinted from *New International Clinics*, 1, Series 2; by permission of the J. B. Lippincott Co.)

grasped, shows expansile pulsation as well as upward thrust. It will seldom be found to move with respirations. If the aneurysm is high up under the diaphragm, or if it points posteriorly, palpation of the sac may be difficult or impossible. Often, on auscultation, a systolic murmur is heard over the mass. In some instances, the patient presents himself with the chief complaint of pulsating abdominal tumor mass (described by one patient as an "extra heart"). The pulsating aneurysmal sac must be differentiated from the throbbing abdominal aorta and from tumor masses overlying and transmitting pulsations of the aorta. In patients where the thickness of the abdominal fat is not too great and the musculature not too rigid, differentiation of an aortic aneurysm from a visceral tumor mass may readily be made if the patient assumes the

knee-chest position. The tumor will fall away from the aorta and no longer transmit the pulsation to the examining hand.

It is well to remember in cases of suspected abdominal aortic aneurysm that a marked pulsation of the aorta is met in cases of extreme anemia, in patients with aortic insufficiency, in hyperthyroidism and in many underweight, neurotic individuals. In these cases it may be possible to grasp the vessel in the hand and the diagnosis of aneurysm is often made. More detailed examination will always show that only an up and down throbbing is present and no lateral expansile pulsation. However, if the aneurysm is completely filled with clotted blood, it may closely simulate a tumor mass and in these cases roentgenologic examination proves invaluable.<sup>43, 44, 45, 46</sup> Many times roentgenograms will reveal a pressure erosion in the vertebral column<sup>47</sup> and avoid an unnecessary laminectomy. This erosion is searched for between the eleventh dorsal and third lumbar segments. The most frequent combination is the erosion of the twelfth dorsal and first lumbar segments.<sup>48</sup>

We have encountered abdominal aneurysms three times, proving the diagnosis in each instance, in 4,058 patients referred to the Cardiac Clinic of the Women's College Hospital during the past eight years. All were encountered in men past 60 years of age, and all were of the arteriosclerotic type.

Another case showing rupture of the aorta with severe abdominal pain and presence of a palpable mass was recently seen by one of us at the Bryn Mawr Hospital.

**Case 6.**—Rupture of the thoracic aorta with dissection, diagnosed gastro-intestinal tract malignancy and perforation.

H. T., colored, female, age 41, was admitted to the hospital, complaining of a sudden, severe, agonizing abdominal pain. Vomiting occurred soon after the onset which was later bloody and was attended by collapse. Examination showed a markedly enlarged heart mostly in the region of the left ventricle, no murmurs, normal rhythm. The abdomen was distended with a nonpulsating, tender, rounded mass in the right upper abdominal quadrant, extending to the right lower quadrant, and about the size of a large grapefruit. Other abdominal areas were quite tender. Peristalsis could be made out in the left upper quadrant but was absent elsewhere. An electrocardiogram showed diphasic T-waves in Leads 1 and 2 and a left axis deviation. Two days later there was recurrence of severe, sudden abdominal pain. The patient quickly developed signs of profound shock and died in 20 minutes.

**Autopsy.**—Body of a colored woman, approximate age 41, quite obese. There was a large area of ecchymosis in the right flank below the costal margin. There was a low midline abdominal scar. On removing the skin, the subcutaneous tissue of the right parietal abdominal wall was diffusely hemorrhagic. There was a subserosal hematoma in the same area. On opening the chest, the right pleural cavity contained a great quantity of serous fluid together with a huge blood clot. The left pleural cavity contained a lesser amount of fluid and clot. The pleural surface of the diaphragm on the right side appeared ecchymotic. There was a diffuse hematoma beneath both right and left parietal pleurae as it joined the visceral pleura at the hilum.

The heart, lungs, and aorta, down to the bifurcation of the common iliacs, were dissected *in toto*. There was noted diffuse hemorrhagic spreading from the posterior mediastinum downward along the aorta retroperitoneally. On opening the aorta, it appeared atheromatous. There was no intimal puckering. There was what appeared to be a small perforation in the upper thoracic aorta with retropleural and retroperitoneal

hemorrhage. The lungs were not adherent and gave no evidence of pathology (right lung 300 Gm., left lung 250 Gm.).

*Heart.*—Pericardium normal. Myocardium hypertrophied and dilated, soft consistency. Valves intact, no separation between the aortic leaflets (430 Gm.).

*Liver.*—1,300 Gm. Appeared normal, gave evidence of passive congestion on section; no other gross pathology. Gallbladder wall was slightly thickened and the gallbladder contained a solitary gallstone.

*Kidneys.*—Right 150 Gm. Left 175 Gm. Showed some slight decrease in cortical substance in proportion to the medulla. There was a slightly generalized fibrosis. There were small retention cysts in the upper pole of both kidneys.

*Spleen.*—100 Gm. Normal size, grayish light pink in color, extremely soft.

*G.-I. Tract.*—Appeared normal with the exception of the sigmoid colon where there were numerous diverticula.

*Uterus* was present and appeared atrophic.



FIG. 6.—Autopsy specimen showing ruptured aorta and pathway formed by dissection.

*Cause of Death.*—Generalized atheromatosis with perforation of the aorta, hemothorax and retroperitoneal dissection.

*Note.*—After fixation in formalin, the heart and aorta were carefully dissected out. The perforation appeared to be about 5 cm. below the arch of the aorta in the posterior surface in correspondence with a deep-seated atheromatous ulceration. From this point the blood appeared to have dissected out the adventitia for a short track, then breaking the adventitia and infiltrating the loose prevertebral tissue in the manner already described (Fig. 6).

**Case 7.**—Thrombosis of the superior mesenteric artery, diagnosed ruptured peptic ulcer.

Hosp. No. 2263: R. A., male, age 44. Well until six hours before admission, when he was awakened from sleep with severe pain in the right lower quadrant. The patient described the pain as a "severe blow." Vomiting occurred several times and this was followed by diarrhea. There were seven bowel movements between 2 A.M. and time of admission to the hospital at 7 A.M. The pain continued, increasing in severity and radiating to the back. On admission, the patient appeared acutely ill. There was dyspnea and

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extreme restlessness from continuous pain. The abdomen was distended with a board-like rigidity. Tenderness was generalized. There was no peristalsis and no masses were palpable. A plain film showed stepladder formation of intestinal obstruction. The pre-operative diagnosis was ruptured peptic ulcer. At operation, thrombosis of the superior mesentery artery was found with intestinal obstruction and gangrene of the ileum (Fig. 7). A cecostomy was performed, but the patient died two hours later.

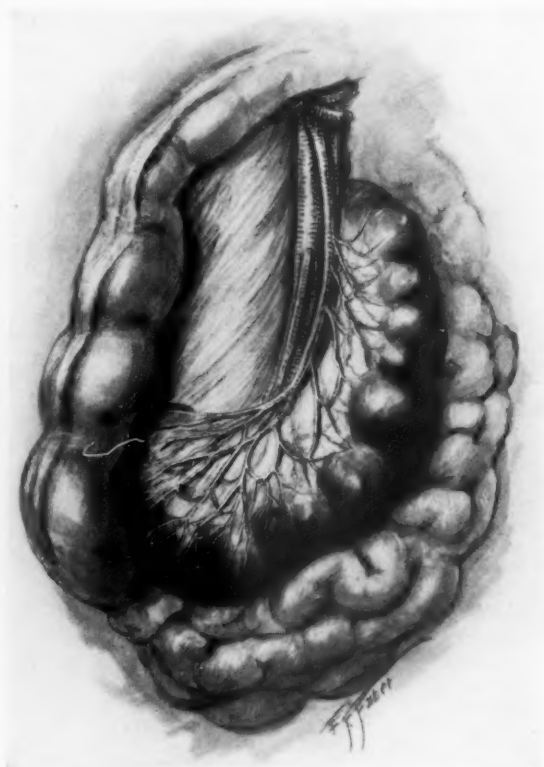


FIG. 7.—Gangrene of intestinal loop following thrombosis of superior mesenteric artery.

*Discussion.*—Embolism or thrombosis of the superior and inferior mesenteric arteries commonly occurs in the presence of endocarditis or arteriosclerosis. Infarction almost always follows and the outcome, particularly when the superior mesenteric artery is involved, is nearly always fatal. An embolus may arise from vegetations in the left side of the heart in cases of bacterial endocarditis, from a thrombus in the auricular appendix in advanced mitral disease with stenosis, and then it may lodge in one of the large branches of the superior mesenteric artery and almost always produces a fatal abdominal picture. Atheromatous degeneration of the arterial wall may lead to the same catastrophe. Rarely, thrombosis of the vein, secondary to acute appendicitis or an inflammatory process in the pelvis, may have the same effect. The resulting infarct, nearly always of the red or hemorrhagic type, usually involves the

lower part of the ileum or jejunum, and this area quickly becomes gangrenous, resulting in a general peritonitis.

As in the case described here, the onset of this condition is usually sudden, with acute, paroxysmal abdominal pain due to the cutting off of the blood supply to the segment of the bowel. Diarrhea is not uncommon. At times, the passage of blood by bowel suggests intussusception. Later, all the signs of obstruction appear with symptoms generally indistinguishable from those caused by internal strangulation. Accurate diagnosis, prior to operation, is

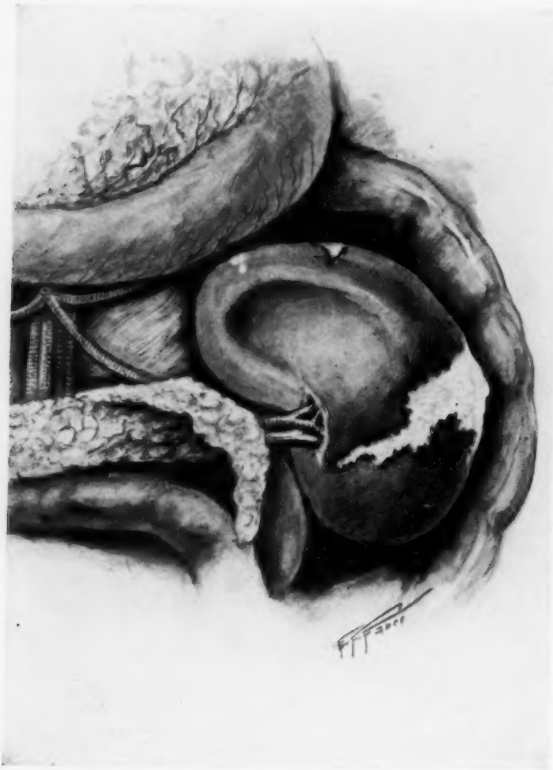


FIG. 8.—Infarct of spleen following embolism in case of subacute bacterial endocarditis.

seldom made in these cases. They are usually diagnosed as acute intestinal obstruction or ruptured peptic ulcer.

**Case 8.**—Subacute bacterial endocarditis, with splenic infarction, causing left upper quadrant pain.

Hosp. No. 3279: R. F. K., male, age 31, was admitted to the Woman's College Hospital, complaining of pain and tenderness in the left upper abdominal quadrant, sudden in onset. Over the course of the previous two months, there had been progressive weakness, pallor and evening temperature of  $100^{\circ}$  F. He had been able to work until a week before admission. The past medical history was positive for rheumatic infection at age of 13. Examination showed temperature  $101^{\circ}$  F., pulse 110, blood pressure 150/40. There



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was stenosis and regurgitation at both mitral and aortic valves. The spleen was palpable and tender. The fingers showed clubbing. A blood culture showed 125 colonies of *Streptococcus viridans* per cubic centimeter. Three weeks later, the patient sat up in bed and died suddenly with all symptoms of cerebral embolism. An autopsy confirmed the diagnosis of cardiac enlargement, aortic and mitral stenosis with superimposed vegetations of subacute bacterial endocarditis. The cause of the attack of acute left upper quadrant pain on admission is suggested by the splenic infarct shown in Figure 8.

*Discussion.*—Subacute bacterial endocarditis is of surgical interest on account of the frequency in this condition of emboli to the abdominal organs with the production of symptoms simulating acute emergencies.<sup>50</sup> The splenic, renal and mesenteric arteries are, perhaps, in the order named, the most common sites for emboli to lodge. In the spleen, the infarct is of the anemic type, often multiple and ranging in size from that of a small pea to an embolus as large as the whole organ. The symptoms vary from none at all to a sudden sharp left upper quadrant pain of the type that brought this patient to the hospital for relief. Rigidity of the muscles over the area is not uncommon, and the pain is usually accentuated by breathing. Wedd<sup>49</sup> reports three cases of infarcted spleen following subacute bacterial endocarditis where celiotomies were performed for a ruptured abdominal viscus. Infection of the area of the infarct by bacteria in the embolus may occur with spread to the peritoneum, and death.

## SUMMARY

The mode of production of abdominal symptoms by the following types of circulatory disorders is reviewed: Congestive cardiac failure with liver enlargement, chronic cardiac compression resulting from calcific pericarditis with enlargement of the liver and ascites, coronary occlusion and angina, abdominal angina, abdominal aortic aneurysm with rupture, rupture of the aorta with dissection, thrombosis of the superior mesenteric artery and embolism. Following the résumé of the record of each typical case, the diagnostic points essential in the detection of the cardiovascular background are discussed.

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DISCUSSION.—DR. ALLEN O. WHIPPLE (New York, N. Y.): I am particularly pleased to have the opportunity of discussing Doctor Rodman's paper, because it appealed to me very much in its conception; and in discussing the matter with him during the past three or four months, I thought that the paper was particularly opportune. So far as I know, this is the first time that these various types of cardiovascular diseases, either of preoperative or postoperative lesions, have been collected and discussed in a paper before this Association.

The analysis of these various lesions and the way in which Doctor Rodman has discussed them show very definitely that he has given this matter real study in conjunction with his associates on the medical services. That brings up one of the points that I wish very emphatically to emphasize, which is the teamwork in the hospital between the man who is interested in cardiovascular disease and the surgical team. We have found it of the greatest help, both in our general surgical service and in the service on the surgery of the extremities under Doctor Darrach.

The constant help of the medical group in evaluating the operative risks in the patients, where the operation is one of choice, has been of the greatest help as well as in the patients where the question comes up as to whether to explore or not to explore, because, as Doctor Rodman has said, at times this is a most important decision. Unless the patient is operated upon, it may be a terrible catastrophe if not operated upon; or if the patient is operated upon with one of these lesions, it may be entirely contraindicated.

There are two points that I wish to emphasize: One is the advantages of oxygen therapy in some of these patients with a damaged myocardium and impaired circulation. We have been impressed with this in several groups of

cases, particularly the thyroid group, and, secondly, with the group of cases in which there is a thoracic lesion associated with the damaged myocardium.

The placing of the patient in an oxygen tent, or even better, in an oxygen room, removes a very real burden from the patient in his first two or three days after operation.

The second point which I wish to emphasize, and I am sure that the group from the Toronto Clinic will speak of this, is the advantage of heparin therapy. We have not had anything like the extensive experience that they have had in Toronto, but we have been tremendously impressed with the efficacy of heparin as a preoperative as well as a postoperative measure, in preventing thrombosis and emboli.

DR. MONT R. REID (Cincinnati): I want to cite one case which will illustrate another abdominal vascular condition which Doctor Rodman did not include in his paper, namely, so-called arteritis nodosa. Recently, a young man, age 33, was sent into the hospital from the receiving ward with the diagnosis of a ruptured peptic ulcer. He was having excruciating pain and there was marked tenderness in the epigastric region. However, he did not appear to be very sick, nor did he have any muscular rigidity of the abdomen. On further questioning, it was learned he had had these pains for several weeks. The operation was deferred. The patient was then studied very carefully on both the surgical and medical services, where all kinds of roentgenologic and laboratory studies failed to reveal any organic lesion. The severe pain persisted. The medical resident, Doctor Shiro, suggested that it might be a case of arteritis nodosa. The diagnosis was eventually confirmed through a biopsy of muscle. The histologic sections of the vessels removed were typical of arteritis nodosa.

One interesting thing about this case was that the patient was given sulfanilamide with extraordinary improvement. The temperature, which had been running around 101° F. before operation, soon became normal. His pain was relieved. It has been a year since this therapy was instituted and the patient still remains apparently well.

DR. ARTHUR M. SHIPLEY (Baltimore): Some years ago there came onto the service of the late Doctor Boggs at City Hospital a Negro, age 30, with a mass in the region of his right kidney. This case was worked up on the medical service and a diagnosis of perinephritic abscess was made. He had had no evidence of aneurysm of the abdominal aorta clinically. He had a large shadow which obscured the aneurysm in the roentgenogram—the aneurysm which was found later. Fortunately for the man and for myself, I used the patient in teaching a small group of students, and I went down on this mass through a small incision. When I came down to the tense area containing the supposed pus, I used a curved Kelley clamp, and showed them how to enter such an area without using a knife. When I thrust the clamp into this mass, I had to pull my head over to one side to keep the spurt of blood from hitting me in the face—then I found myself in the position of the small Dutch boy who stuck his finger in a hole in the dike, and I wondered what I should do next. I introduced a number of sutures around my finger and had the assistant tie these one after the other and finally withdrew my finger without the occurrence of further hemorrhage. Four months later the man died. He had a small aneurysm of his abdominal aorta which had slowly perforated, and what he had also was a secondary surgical aneurysm which simulated, clinically, the findings in a perinephritic abscess. Of course I know what I should have done; I should have put an aspirating needle into this area before using it for a teaching demonstration, and that was a sin of omission which I have not forgotten.



DR. HARVEY B. STONE (Baltimore): It has been said that science consists in the discovery, the verification and the classification of facts. Certainly, I think Doctor Rodman's contribution should be considered a valuable scientific achievement from the standpoint of grouping into a coherent, organized classification these vascular lesions which we, of course, have all known about and worried about for a long while.

I think anyone who is actively engaged in teaching must feel very grateful to Doctor Rodman for presenting this nicely grouped and correlated study of these very important and very confusing conditions. Certainly, for me it will be a much easier task to bring sharply and definitely to the attention of students these various forms of cardiovascular lesions which may be confused with surgical conditions.

I think another thing stands out very clearly from this careful grouping, which is, that of all the various conditions described by Doctor Rodman, one group only requires surgical intervention, namely, embolic or thrombotic lesions involving the blood supply of the intestine, and this sharply distinguishes, from the standpoint of therapy, this one out of all the other vascular complications which may occur.

I suppose every one of us, perhaps, could cite instances in which he has made mistakes either in operating upon a supposed surgical condition which turned out afterward to be a vascular lesion, or the reverse error of failing to operate in the belief that the condition was a vascular lesion but which actually was a surgical condition.

There is one case that I should like to cite which was not covered in Doctor Rodman's very comprehensive recitation indicating the complications that may occur with abdominal aneurysms. In brief, the patient came in with a history of sudden severe shock rendering him unconscious. He was found lying on the ground. Some hours later, he was seen in the hospital by me, and I was unable to make a definite decision as to what was wrong with him. I asked Dr. William Fisher to see him with me, and after considerable uncertainty, we decided that he probably had an acute pancreatitis. I shall not go into his symptoms except to say that they did simulate very closely those of acute, fulminating, hemorrhagic pancreatitis. I explored him and found a pancreas greatly distended and swollen and filled with blood, some free blood in the abdominal cavity, but it was noticed at operation that there was no evidence of fat necrosis. He was simply drained, the wound closed, and he died a few hours later. He had a dissecting aneurysm of the abdominal aorta which had ruptured into the pancreas.

DR. WILLIAM E. GALLIE (Toronto, Canada): I have been injected into this discussion by Doctor Whipple without any previous intention on my part of appearing. I can say, however, that the clinical experiences with heparin, which were reported before this society last year by Doctors Murray and Best, have continued to be most encouraging, and that now a very considerable number of patients with emboli lodging in the great vessels, such as the bifurcation of the aorta into its iliac branches, have been dealt with successfully by the removal of the embolus and subsequent treatment with heparin.

Perhaps more important than these cases of arterial embolism, have been a series of four cases of thrombosis of the mesenteric vein, in which excision of the gangrenous bowel followed by the administration of heparin has resulted in the prompt recovery of the patients without the usual extending thrombosis which almost always terminates these cases. We are naturally enthusiastic, therefore, regarding the usefulness of this drug.



# MEMOIRS

EMMET RIXFORD

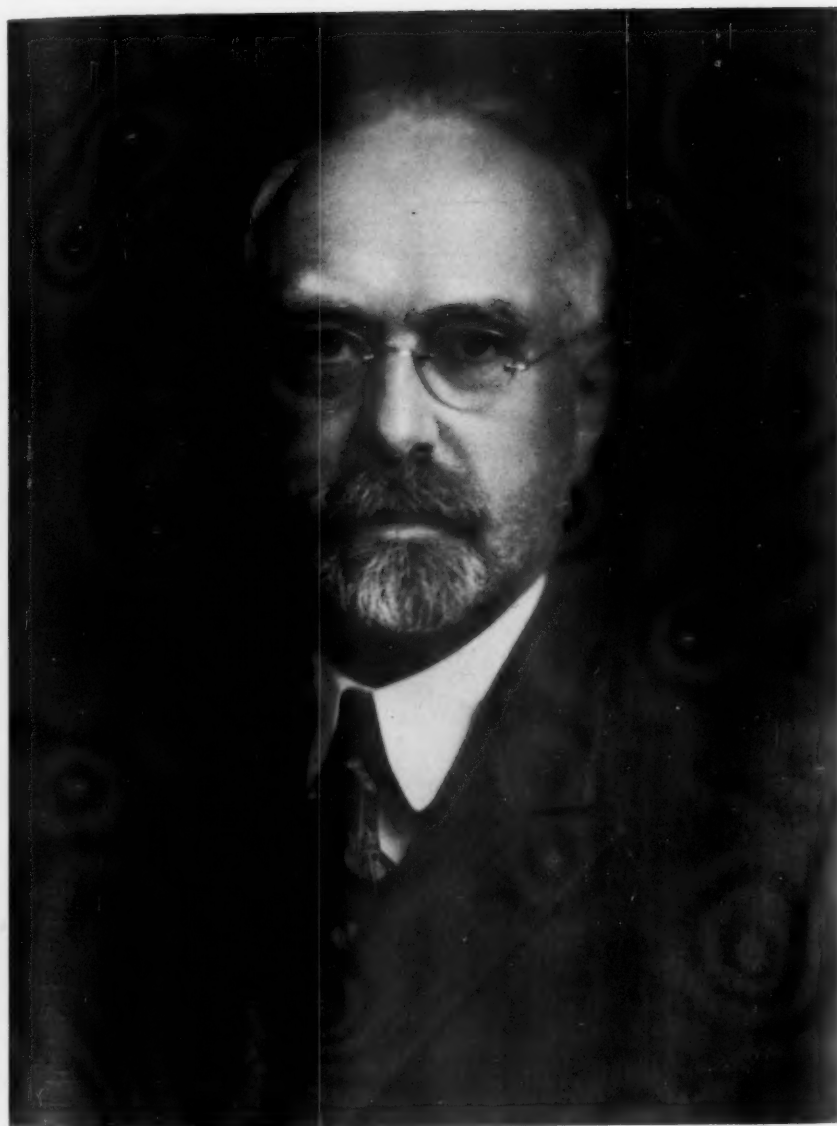
1865-1938

IF TWENTY years or so ago one mentioned San Francisco to a group of doctors, instantly, together with pictures of the Golden Gate and the great earthquake and fire, there would come to their minds the figure of Dr. Emmet Rixford. Doctor Rixford was a part of the West and the West was his. He knew it, he loved it, he helped build it. He walked over it, sailed over its waters, slept under its open skies, climbed its mountains, stood under its trees. He knew its old builders, both the great and the lowly. He talked with them and listened to their stories and told them some of his own; he took care of them and helped relieve their sufferings when they were sick. He knew Western trees and plants and flowers, knew them intimately; he knew the animals and rocks.

Doctor Rixford was born February 14, 1865, in Bedford, a small town in Canada near the Vermont border. His father was a Vermonter, his mother Canadian. His family made axes and scythes in two factories, one in East Highgate, Vermont, and the other in Canada. In 1867, when he was two years old, his parents set out for California in a "side-wheeler," crossed Nicaragua and settled in San Francisco. His father secured a position with the San Francisco Bulletin and was later in the employ of the State Department of Horticulture. Doctor Rixford inherited his love of nature from his father.

He attended the San Francisco public schools and entered the University of California as a student of engineering, graduating in 1887. He often said that his engineering studies had stood him in good stead during his practice of surgery, and had helped him especially to understand the mechanics of fractures, a subject to which he gave particular attention. After having graduated in engineering, he decided to become a doctor and enrolled in the classes of Cooper Medical College, from which he received his doctor's degree in 1891. Among his teachers was Dr. L. C. Lane, a former Navy Surgeon, a Greek and Latin scholar, and the best known surgeon on the Pacific Coast. Lane's clear, cold, classic intellect attracted the young student and after his graduation he became Lane's assistant. He helped him at operations and often acted as nurse and orderly to his patients afterwards. Lane had a busy office in the older business portion of San Francisco; the upper stories of the building were equipped as a small hospital, and here, Doctor Rixford, who had helped operate upon the patients by day, used to take turns with other young men in watching over them at night. Lane never mastered asepsis. He used to consider operation for inguinal hernia unjustifiable, but he was a cool and brilliant operator.

In 1896, Doctor Rixford met Sir William Macewen, of Glasgow, who had come to San Francisco to deliver the first course of Lane Lectures, and ever



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after the influence of Macewen's dominating mind was detectable in his speech and acts.

In 1892, soon after receiving his degree, Doctor Rixford left for the East and spent a year as resident at the New York Hospital for Ruptured and Crippled under the elder Coley. During the summer of 1892, he worked at the Johns Hopkins Hospital in Welch's laboratory. In 1893, he returned to San Francisco and set out to practice surgery on his own account. He was made Adjunct Professor of Surgery at Cooper Medical College in 1893, and Professor of Surgery in 1898.

His publications and his active participation at society meetings and in discussions soon gained him national recognition. He was elected Vice-President of the American Surgical Association in 1905, and was its President in 1928. In this same year, at the request of Dr. Harvey Cushing, he served as Surgeon in Chief, *pro tem.*, of the Peter Bent Brigham Hospital in Boston. He was a member of the Society of Clinical Surgeons and attended their foreign tours regularly. He was a founder of the Pacific Coast Surgical Society and its President in 1932. He belonged to many other societies and held many other offices.

His earlier publications deal with all kinds of surgical topics: hernia, goiter, pancreatitis, gallstones, cancer, *etc.* His most enduring work will probably be the paper in Vol. 1 of the Johns Hopkins Hospital Reports, in which he recognized and, together with Gilchrist, described a new disease, coccidioidal granuloma, and a number of papers on the mechanics and production of fractures, in which he described the physical principles underlying the production of torsion, flexion, buckling and green stick fractures.

The bald recital of his scientific achievements and honors can give but an incomplete idea of this man. His advice and help were sought by patients and colleagues from all over the Pacific Coast. His clinics and colloquia were academic presentations such as few men could offer. Lane Library, the largest medical library in the West, stands as a lasting monument to his love for books and learning. His knowledge of the medical history of the Pacific Coast was wide and accurate. Many of his best writings deal with Western medical history and biography. One regrets that he did not write more of himself, for his hand, no less than Lane's and Cooper's and Toland's, of whom he wrote, guided Western medicine. He knew many of the old pioneers himself; he was close enough to their life, their works and their times to write of them vividly, accurately, understandingly and with justice.

Like these older predecessors of his, he occupied himself with natural history in general and not only with the natural history of disease—inescapably for one who turns to medicine as the most natural avenue for the exercise of an inquiring and logical mind, but who finds it impossible to shut his eyes to the many objects with which a new country surrounds him. He was a true outdoor naturalist; with companions, later with his children, he made pack trips into the Sierra Nevada Mountains and, as he walked, studied the untouched world around him. He climbed the peaks; Mt. Rixford, a 13,000-foot

peak of the Kearsarge Range, is named for him. His early engineering days had awakened in him a peculiar fondness for the spiral. He was fond of studying this curve wherever he met it, and so, in his later years, he collected the shells of land snails and grew to be an authority on them. His town house and his garden, quite near the busy automobile section, were a museum of natural history and an experimental station. After his retirement from teaching, at the age of 65, he found more time for gardening; like his father, who, at the age of 90, began to hybridize orchids that took ten or 20 years to germinate, he went at it with profound interest and zeal. He helped organize the State Horticultural Society and he covered his country place at Los Altos with roses, which he crossed, grafted and raised from seed. He supplied parks and botanical gardens with roses of the original primordial stock which he grew from seed sent him from various countries of Asia.

Doctor Rixford was not a sportsman in the ordinary sense. His thrifty Vermont lineage, I suppose, forbade that, but also his turn of mind, which would rather watch and note the actions of his fellow men and other animals, than struggle with them or kill them. He liked the sea, however; he owned and sailed a large old sloop—the *Annie*. The *Annie* was built in New York in the 70's, and had been a fast sailer in her day. There was a not too well exploded legend that she had been used to convey Boss Tweed from New York to safer quarters when a retreat seemed judicious. Parties of younger doctors and hospital interns, and later his children, manned her until she got too decrepit, when her skipper had her burned at sea rather than let her rot in the mud.

Toward the end of 1937, Doctor Rixford, still vigorous and giving promise of many useful and active years, discovered signs of a carcinoma of the bladder. He died in Boston following a surgical operation, January 2, 1938. His was an unusually varied, useful and active life. He combined the broad interests for all manner of natural phenomena that were characteristic of the best of the earlier American scientists and surgeons with an inquiring, analytic and logical mind, with a retentive, historical and judicious memory and with truly academic learning.

LEO ELOESSER

## SIR THOMAS MYLES

1857-1937

IN THE death of Sir Thomas Myles, an honorary fellow of the American Surgical Association, Ireland has lost one of its most outstanding surgeons. Sir Thomas was well known to many of the members of the American Surgical Association, since he had visited in this country on a number of occa-



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sions, and had made important contributions to the scientific sessions of the Association. Those who had the opportunity of visiting him in Dublin and attending his surgical clinics will always remember him as a great surgeon and teacher and will recall his inspiring personality.

Sir Thomas, son of John Myles of Limerick, was born April 20, 1857. He studied medicine at Trinity College, Dublin, where he received his M.B. and B.Ch. in 1881 and in 1889 his M.D. He served as house surgeon at Steevens Hospital and, in 1885, became a Fellow of the Royal Chirurgical Society of Ireland and was appointed secretary of the Dublin Hospitals Commission. In 1889, he was appointed professor of pathology at the Royal



College of Surgeons of which he was President from 1900 to 1902. For many years he was visiting surgeon to Jervis Street Hospital and later to Richmond Hospital, where the remainder of his active professional life was spent. In 1900, he was made honorary burgess of his native city of Limerick and received the honor of knighthood in 1902. He represented his college on the General Medical Council from 1905 to 1911 and from 1933 until the time of his death. In 1910, he was appointed honorary surgeon in Ireland to King George V, and during the World War, Sir Thomas served as a consulting surgeon to the forces in Ireland. He was elected to honorary membership in the American Surgical Association in 1907. He passed away at his home in Leeson Park, Dublin, July 14, 1937.

The eulogies appearing in the medical journals of Great Britain and Ireland depict Sir Thomas as a man of rare personal charm, equanimity and high scholarly attainments. Sir Thomas possessed a profound knowledge of the surgery of his time and his originality was displayed in many of the contributions by which he advanced surgical progress. He was a man of magnificent physique who was seen by one writer as one who had discovered the secret of perpetual youth. He was most tolerant of the opinions of others and, as another writer has expressed it, "I never saw him out of temper," and "he never forgot a friendly act nor desired to remember an unfriendly one."

I take the liberty of quoting in part a tribute to Sir Thomas from his lifelong friend, Mr. A. B. Mitchell, of Belfast: "Sir Thomas Myles was an outstanding personality in any company. His conversation was always fascinating because of the extraordinary range and accuracy of his knowledge and the simplicity and forcefulness with which he expressed himself. His acquaintance with history was profound. He was one of our greatest Shakespearean scholars, and constantly quoted his favourite author with a fervour and suitability that was most impressive. He was endowed with a colossal memory. He was a voracious reader. A book once read was mastered; he could refer to its individual characters years afterwards as if he had lived and moved amongst them. His wonderful capacity as a teacher of medicine and surgery will never be forgotten till his last pupil has gone to join him in the 'Everlasting Land.' It is not too much to say that one's first visit to 'Tom Myles' Grind' was a revelation. The lucidity, brevity, accuracy, and virility of his descriptions of disease were altogether unique. He prepared more than 1,000 young men for various medical degrees, and for entrance examinations for the Army, Navy, and Indian Medical Services. His pupils have attained the foremost positions in every part of the British Empire. Wherever they went they carried with them not only profound admiration but a deep affection for their great teacher. It is impossible to overestimate his influence upon the lives and character of those who came under his magnetic personality."

The American Surgical Association honors the memory of Sir Thomas Myles and is honored to have on its roster the name of this distinguished surgeon of Ireland.

DONALD C. BALFOUR.

## JOHN LAWRENCE YATES

1872-1938

JOHN LAWRENCE YATES, who died at his home in Milwaukee, November 3, 1938, of an acute throat infection, was born in Milwaukee, Wisconsin, February 27, 1872, the son of Theodore and Marion Wolcott Yates. Doctor Yates was graduated from the Phillips Exeter Academy in 1891, after which



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he attended the Sheffield Scientific School of Yale, receiving the degree of Ph.B. in 1894. He then did postgraduate work for a year at the University of Wisconsin where he received the degree of B.S. in 1895. He was graduated from the Johns Hopkins Medical School in 1899, and was for some time subsequently an assistant in Pathology at that institution. In 1901, he became assistant demonstrator of Pathology at the University of Pennsylvania under Dr. Simon Flexner. Following this, he was for some time associated with Dr. Albert Ochsner at the Augustana Hospital in Chicago and, in 1906, began the private practice of surgery in Milwaukee, Wisconsin, which he continued

until the time of his death. In 1905, he married Katherine Gross, of Harrisburg, Pennsylvania, who, with his sister, Mrs. C. M. Allis, survive him. At the time of his death he was on the surgical staff of several hospitals in Milwaukee and was associate research professor of Oncology at the University of Wisconsin and the Marquette University Medical Schools. He was for many years a fellow of the American Surgical Association, a member of the Association of Thoracic Surgeons, the Society of Clinical Surgeons and many other medical and surgical societies, local and national.

From the above, it is evident that he had led a most active and productive professional life which had earned for him the reputation of being one of America's outstanding surgeons. From his earliest days, he had an unquenchable thirst for investigation of the unknown and this spirit of research influenced and directed all of his professional life. Unlike many interested in research, he was also keenly interested in the human and clinical side of surgery and was devoted to the welfare of his patients, and they in turn devoted to him. No personal sacrifice was ever too great if thereby someone might be benefited. In some of his researches he used himself as an experimental animal and upon one occasion in particular seriously impaired his health. For years he studied and wrote about Hodgkin's disease and related disorders. He made many contributions to surgical literature, notably in connection with the use of drains in peritonitis which he decried, the treatment of gunshot wounds of the chest and latterly cancer, in which he strove to demonstrate the existence of antigens and antibodies. Immediately upon the entrance of the United States into the World War he joined the Medical Corps and ultimately was commissioned a Lieutenant Colonel. He was deeply interested in the treatment of gunshot wounds of the chest and in the quiet periods carried on investigations along these lines in the United States Laboratories at Dijon, but during periods of activity he was always functioning as a surgeon as near the front lines as he was allowed, and to him were usually allotted the bad chest wounds which he handled most skillfully and effectively and taught many others so to do. He was a most patriotic individual and never could quite forgive those whom he thought had slacked their job.

He was possessed of a most charming personality, seriously earnest in everything he undertook but tempered with a joyous nature and a genuine sense of humor which always relieved the drab spots. No one, and they are many, who has ever heard his hearty laugh will forget it. Wherever he went he spread joy and mirth and he was a glorious companion in fun or fight, and the latter he could do when he felt a cause or condition demanded it. His happy nature gave him a cheerful outlook upon life and greatly enhanced his value to his patients, many of whom were cured of their maladies quite as much by his cheery, optimistic manner as by his surgical skill, and the combination was well-nigh perfect.

Honesty, intellectual and actual, was one of his most outstanding qualities and when one asked him a direct question, he received a direct answer.

Loyalty was another superb quality possessed by him in a striking manner,

and never in his life did he fail a friend in time of need. Of his great industry mention has already been made and he played, when he did play, quite as hard as he worked—and he was a grand playboy. To his great host of friends, lay and professional, he was known as “Jack,” which perhaps indicates in some fashion their feeling for him. Rarely, among the host of those who knew him, was he called Doctor Yates but rather Jack Yates. Honesty, Loyalty, Industry, Courage and Ability may be said to have been his outstanding characteristics.

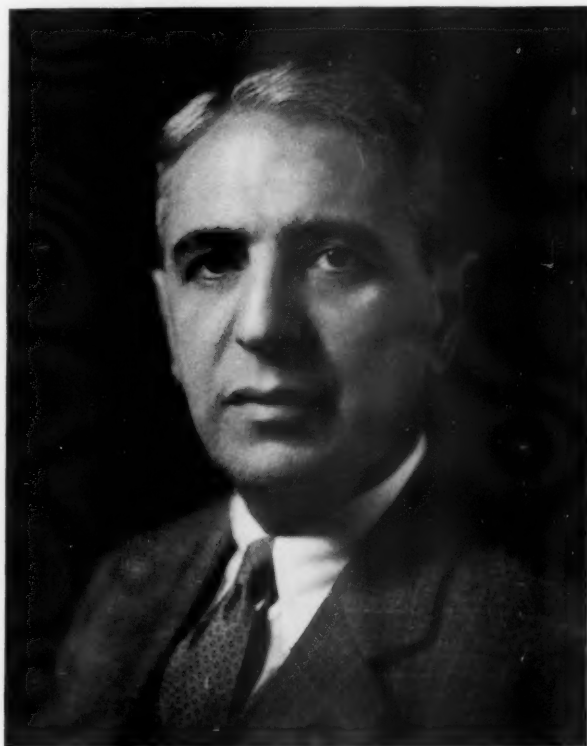
A life full of service to his fellow man, well and effectively lived, he has left a definite impress upon American surgery which will live on, but in the hearts of his patients and many friends, a void that can never be filled.

ARTHUR W. ELTING.

## EDWIN BEER

1876-1938

EDWIN BEER was born in New York City in 1876. He was graduated from Columbia College in 1896, and three years later received his medical degree from the College of Physicians and Surgeons of New York. Upon the completion of his internship at the Mount Sinai Hospital, he went abroad



EDWIN BEER, M.D.

to complete his postgraduate studies in the clinics of Prague, Berlin and Vienna. Shortly after his return to New York, he became associated with the Mount Sinai, Bellevue, Flower, Neurological and the Lenox Hill Hospitals. It was at this latter institution that he developed one of the first cystoscopic departments in the city. In 1910, he was appointed an attending surgeon to the Mount Sinai Hospital and, although in charge of a general surgical service, he became more interested in the field of urology. He served in France during the World War as a Lieutenant Colonel in the U. S. A. Medical Corps. He was a fellow of the New York Surgical Society and its



President upon the occasion of its fiftieth anniversary. He enjoyed fellowship in the American College of Surgeons, the American Urological and the American Surgical Associations, and the International Society of Surgeons. He was a Vice-President of the New York Academy of Medicine and a President of the Medical Board of the Mount Sinai Hospital.

In 1938, upon the occasion of his sixty-second birthday, he was presented with an anniversary volume containing over 70 presentations contributed by his many friends both here and abroad. Although seriously ill at the time with a malady which was to cause his death on August 13, 1938, this volume brought him great joy.

Edwin Beer's medical contributions were innumerable and covered not only the more important problems in many branches of surgery, but especially urology. He was greatly interested in the urologic diseases in the young and perfected one of the first practical cystoscopes for infants. In 1930, he published a monograph on Disease of the Urinary Tract in Children. This was an exhaustive treatise based upon the modern methods of urologic investigation. The crowning event in his brilliant career came in 1927 when, at Brussels, he received the first gold medal given by the International Society of Urology for the use of the Oudin high frequency current in benign bladder tumors, a method which revolutionized their treatment. In 1937, he was awarded the Gold Key by the American Congress of Physical Therapy for his outstanding contributions to the treatment of vesical tumors. His unusual experience in this field enabled him to write an invaluable monograph on Tumors of the Urinary Bladder, which was published in 1937.

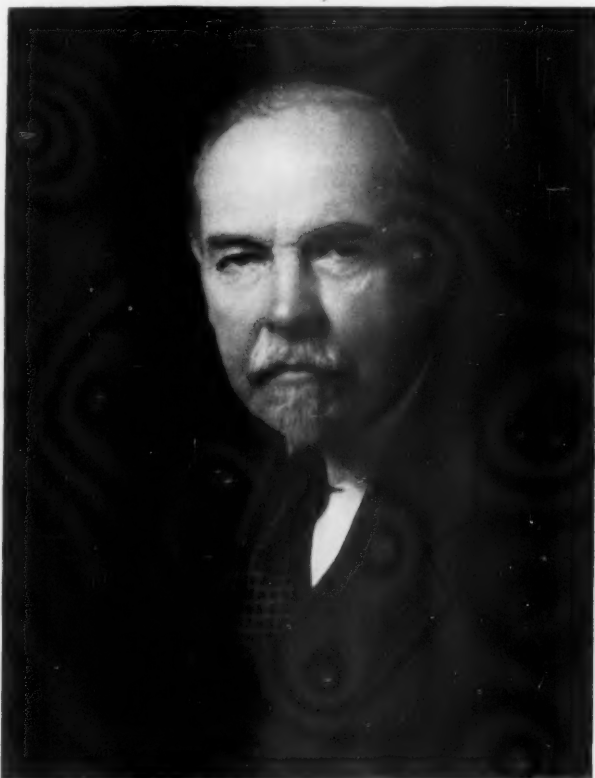
Edwin Beer was a born scholar, endowed with a magnificent intellectual background which gave him an unusual clarity of thought whether in surgery or in the field of economics or sociology. He was a great teacher and his surgical approach to any problem was marked with meticulous attention to the slightest detail, a characteristic which could not help but impress those about him. He was a mental stimulus and an inspiration to the younger generation of surgeons, who came to rely upon his judgment and advice. His untimely death deprived surgery and urology of one of its great, original minds.

RALPH COLP.

## FRANZ J. A. TOREK

1861-1938

FRANZ J. A. TOREK was born April 14, 1861, in Breslau, Germany. At the age of 11, he came to America with his parents and attended the public schools and later the College of the City of New York, graduating at the age of 19. He was elected to Phi Beta Kappa. After teaching English for sev-



FRANZ J. A. TOREK, M.D.

eral years, he studied medicine at the College of Physicians and Surgeons and received the degree of M.D. in 1887.

Following graduation, he served an internship at the German Hospital, now the Lenox Hill Hospital, and remained connected with it until his death, a period of over 50 years. He was a member of the Attending Staff of the New York Post Graduate Hospital, from 1890 to 1915, when he resigned after 25 years of service. He was attending surgeon at St. Mark's Hospital from 1891 to 1905. The history of the New York Skin and Cancer Hospital is closely interwoven with the name of Doctor Torek, for he served on the

Attending Staff from 1890 to 1935, during almost the entire period of independent existence of that institution. After it became merged with the New York Post Graduate Hospital, he was appointed Consulting Surgeon.

He was a member of leading medical and surgical societies, including in addition to the American Surgical Association, the New York Surgical Society, the New York Society for Thoracic Surgery, the American Association for Thoracic Surgery and the German Medical Society. He was an Ex-President of the three latter organizations.

Doctor Torek was a versatile general surgeon. There is no field of surgery into which he did not venture and to which he did not make some worthwhile contribution. Especially, operations requiring technical skill interested him, and this is evident in his writings. The different procedures he developed were always the result of careful planning and practice on the cadaver. His approach to a difficult surgical problem was likewise one of detailed planning and then executing it with an ease and skill which made it appear almost simple. His unusual talents found their greatest application in his treatment of cancer, in which his patience, his deftness and his courage were of inestimable value. Although his publications in this field are limited, it is perhaps principally for his radical cancer operations that he will be remembered by those who were associated with him. His chief service to the public lies in the relief or cure afforded innumerable sufferers from cancer.

His service to the profession may be measured by the training of numerous young surgeons, who were associated with him during the course of years, to be good cancer surgeons. A radical procedure, carried out with neatness and attention to detail, was the point he stressed.

Several operations he developed indicate original thoughts on the subject, and when he presented them they were supported by abundant clinical material.

In 1919, he reported an operation for inguinal hernia, based on the observation that the sac always descends between the vas and vessels of the cord. By high ligation of the neck of the sac and by separating these two structures with the aid of two or three sutures, he sought to overcome this tendency. He was so well satisfied with the method that he continued it throughout his life.

The Torek operation for undescended testicle is being practiced with increased frequency by surgeons throughout the country.

His outstanding contribution to surgery is the operation for carcinoma of the thoracic portion of the esophagus. In November, 1914, he presented the first successful resection. This case has remained famous in the surgical literature because cure resulted and the patient lived for more than 12 years and finally died at the age of 79, of pneumonia. The principles underlying the operation are recognized as fundamental and are being followed by surgeons throughout the world.

In the treatment of his patients, Doctor Torek embodied all the virtues of

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a great surgeon, for he had sympathetic understanding of their mental as well as their physical suffering and he tried to alleviate both.

He had a musical background and was himself an accomplished musician, which contributed much to enrich his life.

Doctor Torek died in Vienna, September 19, 1938, while on a vacation trip undertaken in the hope of finding relief from a cardiac condition. He is survived by his wife, the former Minnie Volkening, and a son and a daughter, as well as several grandchildren.

Because of his personality, his sterling character, his work and his contributions, Doctor Torek will long be remembered and be an inspiration to those who follow after.

He was one of America's great surgeons.

CARL EGGERS.

## BOOK REVIEW

OPERATIVE ORTHOPEDICS. By WILLIS C. CAMPBELL, M.D. 1154 pages with 845 illustrations. C. V. Mosby Co., 1939.

Doctor Campbell's book is a notable contribution to the literature of the modern operative treatment of orthopedic conditions. The author has classified and described the commonly employed operations. The indications and technics are given in full.

He has filled a long felt need for a book to which the busy surgeon can refer for concise descriptions of the various operative technics which can be applied to the condition with which he is confronted.

The choice of the material included in the book is excellent, although a number of operations which have proven to be very satisfactory, in the hands of other surgeons, have been omitted.

The 38 pages devoted to surgical approaches make this book a necessity in the library of every orthopedic surgeon.

ROBERT L. PRESTON.

### EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY

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1833 Pine Street, Philadelphia, Pa.

Contributions in a foreign language when accepted will be translated and published in English.

Exchanges and Books for Review should be sent to James T. Pilcher, M.D., Managing Editor, 121 Gates Avenue, Brooklyn, N. Y.

Subscriptions, advertising and all business communications should be addressed

ANNALS OF SURGERY  
227 South Sixth Street, Philadelphia, Pa.